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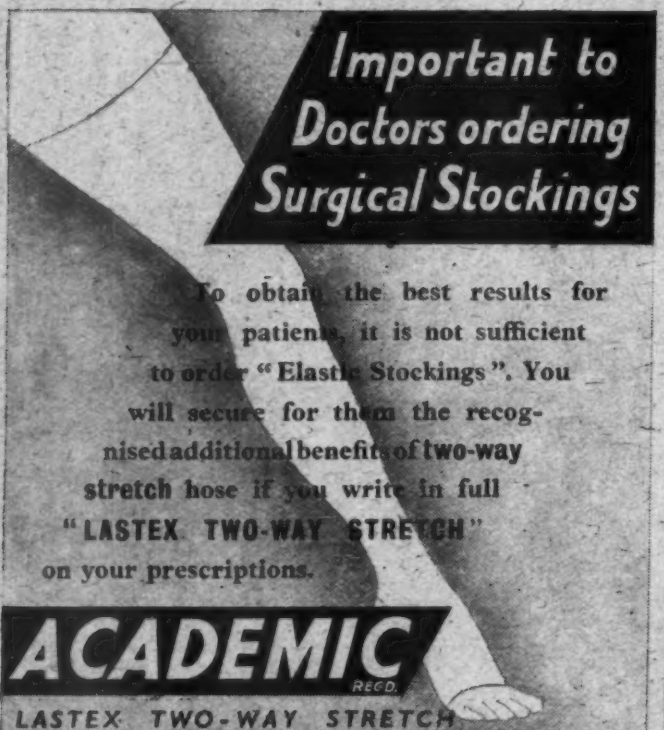

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BRITISH MEDICAL JOURNAL

LONDON SATURDAY APRIL 28 1951

MASS RADIOGRAPHY FINDINGS IN THE NORTHAMPTONSHIRE BOOT AND SHOE INDUSTRY, 1945-6*

BY

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AND

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Recent studies of miniature mass radiography and National Service records (Smith, 1947; Stewart and Hughes, 1949) have revealed the following facts about the boot and shoe industry: (*a*) there is a high incidence of active pulmonary tuberculosis among factory operatives; (*b*) there is more disease in large than in small factories; and (c) the industry tends to recruit men of poor physique. These findings suggest that the high death rate from pulmonary tuberculosis in the industry as a whole (Registrar-General, 1891–1931) is due to selective recruitment, and that the higher rate for factory operatives than for home workers (Registrar-General, 1921–1931) is due to carriers infecting fellow workers.

This hypothesis was put forward in the preliminary report of the present investigation (Stewart and Hughes, 1949). Since then we have re-examined the original mass radiography records and have also collected other data relating to working conditions and to the incidence of pulmonary tuberculosis. A complete report on all this material is not yet available, but two papers, one giving a historical survey of tuberculosis mortality in the printing and shoemaking trades (Cairns and Stewart, 1951) and the other the result of bacteriological sampling of the air in boot and shoe factories (Hirch, 1951), have been accepted for publication since the preliminary report appeared. The purpose of this third paper is to complete the account of the mass radiography survey.

PART I.—COMPARISON OF BOOT AND SHOE WORKERS WITH WORKERS IN OTHER OCCUPATIONS

During its first tour of the county (March 1, 1945, to January 1, 1947) the Northamptonshire mass radiography unit examined 18,660 workers in boot and shoe factories and 23,738 other persons over the age of 14 years (see Table I).

There are minor differences in the data analysed in this and the earlier reports. The first paper (Smith, 1947) refers to all persons examined before June 1, 1946, and the second only to "skilled operatives in boot and shoe factories." In the present paper and in the original report (but not in the interim report) "boot and shoe workers" or "shoemakers" include office and maintenance staff, skilled and unskilled operatives, and all workers in the heel-building and closing factories.

TABLE I.—*Age and Sex Distribution of Workers Examined by Mass Radiography, 1945–6*

Sex	Age Group (in Yrs.)	Occupational Group: Boot and Shoe — No. Examined	Boot and Shoe — Coverage*	Other — No. Examined	Other — Coverage*	Total — No. Examined	Total — Coverage*
			%		%		%
M	14–34	1,863 (19%)	71	4,954 (35%)	69	24,511	70
M	35+	8,284 (81%)		9,410 (65%)			
F	14–34	4,823 (57%)	69	6,866 (73%)	67	17,887	68
F	35+	3,690 (43%)		2,508 (27%)			
Total	All ages	18,660	70	23,738	69	42,398	69

* The number of persons examined expressed as a percentage of the total number on the pay-roll of each factory.

All three reports are based on the records kept by the medical officer in charge of the survey (Dr. M. C. Brough), who was responsible for reading all the films. In the case of serious lung disease, the records incorporate a second professional opinion and, where available, the results of one contemporary sputum test.

The first report includes an occupational analysis of the control group—that is, workers in "other" occupations. Suffice it to say here that half the workers came from engineering, clothing, or leather-dressing factories, and approximately 16% were in professional or clerical occupations.

The coverage (see Tables I, VII, and X) is based on a comparison between the number of persons on the pay-roll of the factories and institutions visited, and the number who attended for examination.

Rather more men than women attended for examination, and shoemakers were better represented than controls, but the only important difference between the two occupational groups was in respect of age: 81% of men and 43% of women in the boot and shoe groups were over the age of 34 years, compared with 65% and 27% respectively in the control group.

In Table II the subjects who were recalled for a large film and those who were not are shown separately. The former includes persons who were found to have tuberculous lesions, other chest diseases, or no disease, and the latter a small number of persons who were suspected of having lung disease but refused to be re-examined. Over 94% of the subjects showed no radiological evidence of disease and less than 0.1% refused to be re-examined.

*Further report of an investigation initiated by representatives of the boot and shoe industry and public health authorities in Northamptonshire, and financed by the Medical Research Council.

†With a grant from the Medical Research Council.

TABLE II.—*Incidence of Tuberculous and Non-tuberculous Lung Diseases*

Disease Category		Occupational Group							
		Boot and Shoe				Other Occupations			
		Males		Females		Males		Females	
Main Group	Subgroup	No.	%	No.	%	No.	%	No.	%
Pulmonary tuberculosis*	Active	71 (*32*)	0·70	54 (*6*)	0·63	41 (*17*)	0·29	60 (*7*)	0·64
	Quiescent	369	3·64	199	2·34	397	2·76	139	1·48
Other diseases*	Pneumoconiosis	2†	0·02	—	—	14	0·10	—	—
	Other lung	71	0·70	22	0·26	129	0·90	30	0·32
	Cardiovascular	35	0·35	6	0·07	37	0·26	25	0·27
	Undiagnosed‡	5	0·04	7	0·08	4	0·03	6	0·06
Nil	Large film	27	0·27	33	0·39	40	0·28	39	0·42
	Small film	9,567	94·28	8,192	96·23	13,702	95·38	9,075	96·81
Total		10,147	100	8,513	100	14,364	100	9,374	100

* Including previously notified persons who were recalled for large films.
† Both men were ex-miners.
‡ Recalled for large film, but failed to attend.
Figures in italics indicate cases with tubercle bacilli in sputum (single examination at time of survey).

Non-tuberculous Disease

Hitherto, no mass radiography statistics relating to non-tuberculous disease among shoemakers have been published. It is necessary, however, to consider these, since a high rate of tuberculosis in an industry could be due to dust disease.

In spite of being older, the shoemakers had no more non-tuberculous disease than the controls. Cardiovascular lesions were relatively uncommon among female boot and shoe workers, but in other respects there was little difference between the two occupational groups. Two of the male shoemakers showed radiological evidence of pneumoconiosis, but since they were both ex-miners it is clearly unrealistic to attribute this to leather dust.

The figures are in line with the fact that shoemakers, in spite of having a high tuberculosis mortality, have a low mortality from other lung diseases. In this respect they offer a striking contrast to potters, tin-miners, and other workers exposed to a silica-dust hazard (Registrar-General, 1891–1931 ; Collis, 1925 ; Cairns and Stewart, 1951).

Tuberculous Disease

In the earlier reports, only "newly discovered active tuberculosis of the lungs in persons who require to stay off work for treatment" was considered. To discover why this type of case was exceptionally common among shoemakers, who do not suffer from pneumoconiosis, several lines of inquiry must be followed. It has, for instance, been suggested that working conditions in boot and shoe factories favour spread of the disease. However, tuberculosis might have been unduly common solely because the trade had recruited an exceptionally large number of tuberculous subjects. Workers who had already been notified were automatically excluded from the newly discovered active group, but conceivably the latter was wholly composed of persons who, though not notified, had in fact developed the disease before entering the industry. Possibly, also, shoemakers are more susceptible to infection than other workers and therefore more liable to develop overt disease. These hypotheses are not mutually exclusive, and to give each its due weight it is necessary to consider five overlapping categories of tuberculous disease: active and quiescent, previously notified and newly discovered, and cases with tubercle bacilli in the sputum.

All Forms of Disease

Radiological evidence of pulmonary tuberculosis was detected in 1,330 cases. In 1,104 of these the disease was quiescent, and in 226 it was active. The former group included 89 previously notified persons, and the latter 15 previously notified and 62 with tubercle bacilli in their sputum. All forms of the disease were more common among shoemakers than controls, but the disparity varied with age, sex, and clinical condition (see Table III).

Quiescent Disease (Newly Discovered and Previously Notified)

Unless tuberculin tests have been made, it is impossible to estimate the infection rate in any one population ; but the *relative* rate of infection in two populations can be judged by comparing the percentage of persons among them who

TABLE III.—*Incidence of Active and Quiescent Tuberculosis*

Age Group (Yrs.)	Sex	Occupation	Workers Examined	Pulmonary Tuberculosis									
				Active				Quiescent				All Cases	
				Newly Discovered		Previously Notified		Newly Discovered		Previously Notified			
				No.	%	No.	%	No.	%	No.	%	No.	%
14–34	M	Boot and shoe	1,863	12 (*2*)	0·64	3 (*2*)	0·16	43	2·31	4	0·21	62 (*4*)	3·33
		Other	4,954	8 (*1*)	0·16	1	0·02	77	1·55	12	0·24	98 (*1*)	1·98
	F	Boot and shoe	4,823	48 (*6*)	1·00	—	—	84	1·74	10	0·21	142 (*6*)	2·95
		Other	6,866	54 (*6*)	0·79	—	—	78	1·14	3	0·04	135 (*6*)	1·97
35+	M	Boot and shoe	8,284	50 (*25*)	0·60	6 (*3*)	0·07	288	3·48	34	0·41	378 (*28*)	4·56
		Other	9,410	28 (*14*)	0·30	4 (*2*)	0·04	292	3·10	16	0·17	340 (*16*)	3·61
	F	Boot and shoe	3,690	5	0·14	1	0·03	97	2·63	8	0·22	111	3·01
		Other	2,508	6 (*1*)	0·24	—	—	56	2·23	2	0·08	64 (*1*)	2·55
All ages	M	Boot and shoe	10,147	62 (*27*)	0·62	9 (*5*)	0·09	331	3·26	38	0·37	440 (*32*)	4·34
		Other	14,364	36 (*15*)	0·25	5 (*2*)	0·03	369	2·57	28	0·19	438 (*17*)	3·05
	F	Boot and shoe	8,513	53 (*6*)	0·62	1	0·01	181	2·13	18	0·21	253 (*6*)	2·97
		Other	9,374	60 (*7*)	0·64	—	—	134	1·43	5	0·05	199 (*7*)	2·12

Figures in italics indicate cases with tubercle bacilli in sputum.

have not knowingly suffered from the disease but who show healed and active lesions. In the present instance, since only one person was responsible for the complete set of records, the "newly discovered quiescent cases" can be assumed to be proportional to the number of healthy tuberculin reactors in the two occupational groups.

There was a higher proportion of cases of quiescent newly discovered tuberculosis among the men than among the women, and more among the shoemakers than among the controls (see Table III). These differences are partly due to differences in the age structure of the four groups, but they cannot be wholly explained in this way. For example, when the subjects were divided into two age groups it was found that 2.31% of male and 1.74% of female boot and shoe workers under the age of 35 years were included in the relevant category, compared with 1.55% of male and 1.14% of female controls. These differences are statistically significant, and similar ones exist in the older age group (see Table III). From this it can be inferred that the shoemakers had been more exposed to infection than the controls rather than more liable to succumb when infected.

Previously Notified Disease (Active and Quiescent)

Men and women who take up work after being treated for tuberculosis do so knowing that they are physically handicapped. Hence the number of previously notified cases in a given occupational group is a measure of conscious selective recruitment. The proportion of these cases found to be suffering from active disease at any given time is also an indication of the breakdown rate after apparent recovery.

In the shoemaking group 0.46% of the men and 0.22% of the women had already been notified as cases of pulmonary tuberculosis, compared with 0.22 and 0.05% of male and female controls. The proportion of active cases in the previously notified group was distinctly higher for men (17.5%) than for women (4.2%), but approximately the same for male and female shoemakers (15.2%) and men and women in other occupations (13.2%).

cases (0.09 and 0.03%) and partly to an excess of newly discovered cases in the older age group (0.60 and 0.30%), but chiefly to the fact that the incidence of newly discovered cases in the younger age group was four times as high for shoemakers as for controls (0.64 and 0.16%).

In theory, an exceptionally large number of newly discovered cases of active pulmonary tuberculosis in the boot and shoe industry could be due solely to choice of this trade by persons who were conscious of ill-health but unaware that the cause was tuberculosis. There are, however, several reasons why this is unlikely. For instance, although young men move relatively easily from one industry to another, they usually suffer from an acute form of tuberculosis which is soon incompatible with work. Older men tend to have a more chronic type of disease, but they are relatively immobile, because change of work at that stage involves loss of status and reduction in earnings. On the other hand, since the boot and shoe industry undoubtedly attracts men of poor physique, some of the men with newly discovered active lesions may have entered the industry after developing the disease. Since persons with chronic lesions are likely to be carriers, the attack rate may also be unduly high among shoemakers.

To obtain further evidence on this last point, the following procedure was adopted. First the original radiographs (large films) of the active cases were reassembled. Then an independent witness* who was not told the age, sex, or occupation of the subjects, or whether they had already been notified, was asked to classify these films as follows:

Group I.—Cases showing radiological evidence of recent infiltration of otherwise healthy lungs.†

Group II.—Intermediate between I and III.

Group III.—Cases showing radiological evidence of old-standing disease, with or without signs of recent exacerbation.

When the classification was completed it was found that within the group of active cases there were no occupational differences in the radiological grading. There were, however, marked sex differences, nearly 90% of the women having recently acquired lesions, compared with only a quarter of the men (see Table IV). Finally, the average age of the subjects, and the number of persons with tubercle bacilli in the sputum, were lowest in Group I and highest in Group III.

TABLE IV.—*Radiological Classification of Cases of Active Tuberculosis*

Sex	Occupational Group	Total Cases		*X*-ray Group									
				Group I				Group II				Group III			
				Cases		Age in Yrs.		Cases		Age in Yrs.		Cases		Age in Yrs.	
		No.	%	No.	%	Mean	S.D.	No.	%	Mean	S.D.	No.	%	Mean	S.D.
M	Boot and shoe	71 (*32*)	100	18 (*4*)	25	33·6	5·9	21 (*10*)	30	44·4	3·6	32 (*18*)	45	50·3	5·3
	Other	41 (*17*)	100	11 (*1*)	27	30·7	5·8	12 (*5*)	29	44·8	5·0	18 (*11*)	44	52·4	5·4
F	Boot and shoe	54 (*6*)	100	48 (*3*)	89	23·8	3·3	6 (*3*)	11	31·7	4·4	—	—	—	—
	Other	60 (*7*)	100	52 (*5*)	87	21·2	2·3	8 (*2*)	13	36·0	3·8	—	—	—	—

Figures in italics indicate cases with tubercle bacilli in sputum.

The distinctions between men and women are probably due to economic factors, and between shoemakers and other workers to the nature of the work performed. As shoemaking does not demand strenuous physical exertion, skilled men who develop tuberculosis find it relatively easy to return to their own occupation. For the same reason men from heavy industries may take up shoemaking after contracting the disease. It was unfortunately not possible to discover how many of the previously notified men attending the mass radiography survey were shoemakers before notification and how many had subsequently migrated into the industry.

Active Disease (Newly Discovered and Previously Notified)

In addition to the newly discovered cases of active pulmonary tuberculosis described in the earlier reports, there were a few previously notified cases with active disease. Taking these two types of case together there was no difference between the women in the two occupational groups, but the rate for male shoemakers was over twice as high as the rate for other men (see Tables II and III). This difference was due partly to an excess of previously notified

This attempt to group the active cases according to the age of the disease process, on *x*-ray evidence alone, has obvious weaknesses, and it is unlikely that two observers would have agreed in all cases (Birkelo *et al.*, 1947; Fletcher and Oldham, 1949). There are, however, several cogent reasons why the classification can be accepted as generally true of the group, in spite of possible errors in the placing of a few individuals. In the first place, the different results for the two sexes are such as would have been expected. Secondly, the results for the two occupations, where no

*We are indebted to Dr. W. T. Bermingham, who succeeded Dr. Brough as medical officer in charge of the mass radiography unit after the first survey was completed, for this part of the investigation.

†For the purpose of this investigation, a calcified Ghon or Assmann focus was not regarded as evidence of previous disease.

differences were to be expected, are, in fact, identical. Thirdly, there is a definite and steady age gradient. Fourthly, there is an equally marked increase from group to group in the number of cases with tubercle bacilli in the sputum. Finally, none of the previously notified cases was mistaken for recently acquired disease. Hence, the admitted weaknesses of this method of grading, from the point of view of individual diagnosis, do not invalidate its use for showing what very different types of disease are included in the category "newly discovered active cases revealed by mass radiography," and indicating their approximate proportions.

Since the overall incidence of newly discovered active cases, and also the incidence of recently acquired and old-standing lesions, were greater among the shoemakers than among the controls, there must have been a high attack rate as well as a high carrier rate in the boot and shoe factories.

PART II.—COMPARISON BETWEEN DIFFERENT GROUPS OF SHOEMAKERS

In the interim report of the present investigation it was suggested that the relationship between factory size—that is, total working population—and incidence of newly discovered active cases of pulmonary tuberculosis might be due to the fact that, given similar working conditions, including spacing of operatives, the risk of contracting the disease was proportional to the number of persons per room. This hypothesis assumes (*a*) that it is possible for carriers to infect fellow workers, (*b*) that carriers are randomly distributed in boot and shoe factories, and (*c*) that there are usually more persons per room in large factories than in small ones.

In order to obtain further evidence on these points the statistics for boot and shoe operatives were analysed in terms of factory size, occupation, and region. The following definitions were also adopted:

Attack Rate.—The number of newly discovered active cases of pulmonary tuberculosis in *X*-ray Group I per stated number of workers.

Carrier Rate.—The number of cases of active pulmonary tuberculosis (newly discovered and previously notified) in *X*-ray Groups II and III per stated number of workers.*

1. Factory-size Analysis

Carrier and Attack Rates in Factories of Different Sizes

In Tables V and VI, male and female shoemakers are shown in five factory-size groups. Table V includes all cases with tuberculous lesions (active and quiescent) and also distinguishes the previously notified from the newly discovered cases.

In the interim report males and females were not discussed separately. However, Table V shows that the correlation between factory size and incidence of newly discovered active pulmonary tuberculosis holds true for both sexes. It also shows that the distribution of previously notified and quiescent cases is not influenced by factory size.

In Table VI the active cases, with and without tubercle bacilli in the sputum, have been placed in the three *x*-ray groups. Estimated attack rates and carrier rates for the five factory-size groups, calculated from these basic data, are also included.

*According to this definition, a carrier is "a person known to have active pulmonary tuberculosis and suspected of having had it for some time." Originally a more rigid definition was used which included only persons in *X*-ray Group III known to have tubercle bacilli in their sputum. Whichever definition is used, the results are essentially the same, but it is more convenient numerically to express the relationship between carriers and "victims" in terms of the index which incorporates the larger number of cases.

TABLE V.—*Shoemakers Only. Factory-size Analysis. Incidence of Active and Quiescent Tuberculosis*

Factory-size Groups (Working Population)	Workers Examined		Cases of Pulmonary Tuberculosis				
			No.		Rates		
	No.	Over 35 Yrs. %	Active	Quiescent	A/ND	Q/ND	P/N
Males:					%	%	%
1–100 ..	1,936	82	9 (*3*)	67 (*4*)	0·31	3·25	0·36
101–200 ..	2,443	80	15 (*2*)	93 (*7*)	0·53	3·52	0·37
201–350 ..	2,341	81	17 (*3*)	75 (*8*)	0·60	2·86	0·47
351–600 ..	1,712	79	11	73 (*12*)	0·64	3·56	0·70
Over 600 ..	1,715	77	19 (*1*)	61 (*7*)	1·05	3·15	0·47
Total ..	10,147	80	71 (*9*)	369 (*38*)	0·61	3·26	0·46
Females:							
1–100 ..	1,505	45	7 (*1*)	32 (*6*)	0·40	1·73	0·47
101–200 ..	2,037	44	8	45 (*3*)	0·39	2·06	0·15
201–350 ..	1,773	44	11	47 (*6*)	0·62	2·31	0·34
351–600 ..	1,319	42	10	40 (*2*)	0·76	2·88	0·15
Over 600 ..	1,879	40	18	35 (*1*)	0·96	1·81	0·05
Total ..	8,513	43	54 (*1*)	199 (*18*)	0·62	2·13	0·22

A/ND = Active newly discovered. Q/ND = Quiescent newly discovered P/N = Previously notified. Figures in italics indicate previously notified cases.

TABLE VI.—*Shoemakers Only. Factory-size Analysis. Estimated Attack Rates and Carrier Rates for Pulmonary Tuberculosis*

Factory-size Groups (Working Population)	Workers Examined		*X*-ray Groups			Estimated Attack Rate*	Estimated Carrier Rate*
	No.	Over 35 Yrs.	Group I	Group II	Group III		
Males:		%				%	%
1–100 ..	1,936	82	1 (*1*)	4 (*3*)	4 (*1*)	0·05	0·41
101–200 ..	2,443	80	3	3	9 (*4*)	0·12	0·49
201–350 ..	2,341	81	4	5 (*2*)	8 (*6*)	0·17	0·56
351–600 ..	1,712	79	4	5 (*3*)	2 (*1*)	0·23	0·41
Over 600 ..	1,715	77	6 (*3*)	4 (*2*)	9 (*6*)	0·35	0·76
Total ..	10,147	80	18 (*4*)	21 (*10*)	32 (*18*)	0·18	0·52
Females:							
1–100 ..	1,505	45	5	2	—	0·33	0·13
101–200 ..	2,037	44	8 (*1*)	—	—	0·39	—
201–350 ..	1,773	44	9 (*1*)	2 (*2*)	—	0·51	0·11
351–600 ..	1,319	42	9	1	—	0·68	0·08
Over 600 ..	1,879	40	16 (*1*)	2 (*1*)	—	0·85	0·11
Total ..	8,513	43	47 (*3*)	7 (*3*)	—	0·55	0·08

* Estimated attack rates based on cases in *X*-ray Group I; estimated carrier rates based on cases in *X*-ray Groups II and III.
Figures in italics indicate cases with tubercle bacilli in sputum.

These figures show that both the attack rate and the carrier rate for males were lowest in factories with fewer than 100 workers and highest in factories with over 600 workers. The numbers are too small to assess the significance of the differences between each factory-size group, but, if factories with over and under 600 workers are compared, the difference in the two attack rates is found to approach statistical significance

$$\left(\text{i.e., } \frac{\text{the observed difference}}{\text{standard error of the difference}} = 1.9\right)$$

The difference between the two corresponding rates is not statistically significant. In the case of females the attack rate also increased with size of factory. The gradient was less steep than in the case of men, but for factories with over 600 workers the attack rate was two and a half times as high as the rate for factories with fewer than 100 workers.†

Only tentative conclusions may be drawn from these results. The steady rise in the attack rate suggests that factory size has an important influence on the risk of contracting tuberculosis. On the other hand, it is uncertain whether the rise in the male carrier rate was due

†It should be noted here that there is even less segregation of male and female operatives in boot and shoe factories than the occupational grouping suggests (see Tables VIII and IX). There is, for instance, a traditional association between clickers and closers and between finishers and shoe-room workers, and in several factories all the workers are housed in the same room. It is therefore reasonable to assume that many of the young women with active tuberculosis had been in contact with male carriers.

to the fact that carriers were not randomly distributed or to the impossibility of making a clear-cut distinction between carriers and victims. So far as they go, the female rates support the latter explanation.

Numerical and Spatial Arrangement of Workers

No record of the internal working arrangements in boot and shoe factories was made at the time of the mass radiography survey. When, however, it was found that factory size was influencing the distribution of newly discovered active cases the factories were revisited and the following information obtained: (*a*) the number of separate workrooms in each factory; (*b*) the number of workers (in the main occupational groups) in each room; and (*c*) the floor area of each workshop.

In a representative sample of 25 factories the actual distance between typical groups of workers was also measured. From these data mean values for workers per room, floor space per worker, and distance between adjacent workers were obtained for the five factory-size groups and the six clearly defined occupations (see Tables VII and X). This analysis revealed a positive correlation between factory size and number of workers

TABLE VII.—*Shoemakers Only. Factory-size Analysis. Numerical and Spatial Arrangement of Workers*

Factory-size Groups (Working Population)	No. of Factories	Workers Examined		Numerical and Spatial Arrangement of Workers (Mean Values)		
		No.	Coverage*	Persons per Room	Floor Area per Worker	Distance Between Workers
			%		sq. ft. (m.²)	ft. (m.)
1–100 ..	100	3,441	70	14·7	111 (10·31)	6·5 (1·98)
101–200 ..	43	4,480	68	34·9	93 (8·64)	6·2 (1·89)
201–350 ..	23	4,114	73	61·0	104 (9·66)	6·4 (1·95)
351–600 ..	9	3,031	66	70·8	90 (8·36)	5·9 (1·80)
Over 600 ..	6	3,594	72	97·3	77 (7·15)	5·5 (1·68)
Total ..	181	18,660	70	37·1	95 (8·83)	6·1 (1·86)

* The number of workers examined expressed as a percentage of the total number on the pay-roll of each factory.

per room. Thus the third assumption made in the interim report (that there are usually more persons per room in large than in small factories) was clearly justified. It was also found that the workshops in large factories tend to be more congested than the workshops in small factories. Hence the risk of contracting diseases due to droplet infection is likely to be greater in the former.

2. Occupational Analysis

Attack Rates and Carrier Rates in Boot and Shoe Factories

There are six clearly defined occupational groups in boot and shoe factories. In four of these (clicking, lasting, finishing, and rough stuff) male workers are in a majority, and in two (closing and shoe rooms) the majority are women (see Table VIII).

The first report of the mass radiography survey showed that the incidence of newly discovered active pulmonary tuberculosis was exceptionally high in the clicking, lasting, and finishing, but not in the rough-stuff, closing, or shoe-room departments. Since workers in closing and shoe rooms are usually women, it is not surprising that the rates for newly discovered active cases in these departments were not significantly different from those for women in the control group (see Table III). In the rough-stuff departments, however, it was the male workers who were found to have significantly lower rates than the other men (see Smith, 1947, also Table VIII). To discover why male rough-stuff workers (most of whom are sole-cutters) are an exception to the general rule, the occupational

TABLE VIII.—*Shoemakers Only. Occupational Analysis. Incidence of Active and Quiescent Tuberculosis*

Sex	Occupation	Workers Examined		Tuberculosis Lesions				
		Total No.	Over 35 Yrs.	No.		Rates		
				Active	Quiescent	A/ND	Q/ND	P/N
			%			%	%	%
Males	Clickers	1,975	76	16 (*1*)	89 (*15*)	0·76	3·75	0·81
	Closers	46	68	2 (*1*)	1	2·17*	2·17*	2·17*
	Rough stuff	1,091	86	3	35 (*3*)	0·27	2·93	0·27
	Lasters	3,505	80	26 (*4*)	123 (*7*)	0·63	3·31	0·31
	Finishers	1,988	86	16 (*1*)	73 (*7*)	0·75	3·32	0·40
	Shoe room	228	93	1	11 (*2*)	0·44*	3·95*	0·88*
	Other	1,314	83	7 (*2*)	37 (*4*)	0·38	2·51	0·46
	Total	10,147	80	71 (*9*)	369 (*38*)	0·61	3·26	0·46
Females	Clickers	172	41	1	6 (*1*)	0·58*	2·91*	0·58*
	Closers	4,999	45	28 (*1*)	127 (*12*)	0·54	2·30	0·26
	Rough stuff	493	55	1	10 (*1*)	0·20*	1·83*	0·20*
	Lasters	407	49	6	9 (*2*)	1·47*	1·72*	0·49*
	Finishers	101	44	—	4	—	3·96*	—
	Shoe room	923	47	7	30 (*2*)	0·76	3·03	0·22
	Other	1,418	32	11	13	0·78	0·92	—
	Total	8,513	43	54 (*1*)	199 (*18*)	0·62	2·13	0·22

A/ND = Active newly discovered. Q/ND = Quiescent newly discovered. P/N = Previously notified. * Figures based on fewer than 500 workers. Figures in italics indicate previously notified cases.

groups were reanalysed in terms of previously notified and newly discovered cases, *x*-ray groups and numerical and spatial arrangement of workers. Table VIII shows that the incidence of newly discovered quiescent cases was actually lower among male rough-stuff workers than among male clickers, lasters, or finishers, though this difference is slight and not statistically significant. It is unlikely, therefore, that the low rate for newly discovered active cases among rough-stuff workers was due to a high level of acquired resistance to tuberculosis. The proportion of previously notified male cases was less in the rough-stuff rooms than elsewhere. Possibly tuberculous subjects prefer working in other departments, since the rough-stuff rooms are notoriously dusty, are often situated in a basement or semi-basement, and include one of the few shoemaking occupations which can be described as moderately heavy work—namely, sole-cutting.

Table IX shows that, in the male occupational groups, the number of active cases with "old" lesions—that is, *X*-ray Groups II and III—and the number with "new"

TABLE IX.—*Shoemakers Only. Occupational Analysis. Estimated Attack Rates and Carrier Rates for Pulmonary Tuberculosis*

Sex	Occupation	Workers Examined		Cases of Active Tuberculosis				
		Total No.	Over 35 Yrs.	*X*-ray Groups			Estimated Attack Rate†	Estimated Carrier Rate†
				I	II	III		
			%				%	%
Males	Clickers	1,975	76	4	6 (*2*)	6 (*5*)	0·20	0·61
	Closers	46	68	—	1 (*1*)	1 (*1*)	—	4·35*
	Rough stuff	1,091	88	—	1	2 (*1*)	—	0·27
	Lasters	3,505	80	8 (*2*)	7 (*5*)	11 (*7*)	0·23	0·51
	Finishers	1,988	86	4 (*1*)	4 (*2*)	8 (*4*)	0·20	0·60
	Shoe room	228	93	—	1 (*1*)	—	—	0·44*
	Other	1,314	83	2 (*1*)	1 (*1*)	4 (*2*)	0·15	0·38
	Total	10,147	80	18 (*4*)	21 (*10*)	32 (*18*)	0·18	0·52
Females	Clickers	172	41	1	—	—	0·58*	—
	Closers	4,999	45	24 (*1*)	4 (*2*)	—	0·48	0·08
	Rough stuff	493	55	1	—	—	0·20*	—
	Lasters	407	49	5 (*1*)	1 (*1*)	—	1·23*	0·25*
	Finishers	101	44	—	—	—	—	—
	Shoe room	923	47	7	—	—	0·76	—
	Other	1,418	32	10 (*1*)	1	—	0·71	0·07
	Total	8,513	43	48 (*3*)	6 (*3*)	—	0·56	0·07

* Figures based on fewer than 500 workers.
† Estimated attack rates based on cases in *X*-ray Group I; estimated carrier rates based on cases in *X*-ray Groups II and III.
Figures in italics indicate cases with tubercle bacilli in sputum.

lesions, that is, *X*-ray Group I—bear a fairly constant relationship to one another. As the male rough-stuff workers included relatively few cases in *X*-ray Groups II and III and none in Group I, it is likely that both the carrier rate and the attack rate were unusually low in this department. Table X also shows that there are

TABLE X.—*Shoemakers Only. Occupational Analysis. Numerical and Spatial Arrangement of Workers*

Factory Department	Workers Examined		Numerical and Spatial Arrangement of Workers (Mean Values)		
	No.	Coverage*	Workers per Room†	Floor Area per Worker	Distance Between Workers
		%		sq. ft. (m.²)	ft. (m.)
Clicking ..	2,147	73	53	86 (7·99)	5·3 (1·62)
Closing ..	5,045	72	64	40 (3·72)	3·0 (0·91)
Rough stuff ..	1,584	70	46	140 (13·01)	7·6 (2·32)
Lasting ..	3,912	73	63	84 (7·80)	4·8 (1·46)
Finishing ..	2,089	72	66	94 (8·73)	4·7 (1·43)
Shoe room ..	1,151	72	42	133 (12·35)	5·9 (1·80)
Total ..	15,928	72	57	95 (8·83)	6·1 (1·86)

* The number of workers examined expressed as a percentage of the total number on the pay-roll of each factory. (N.B.—The total number on the pay-roll is an *estimate*, based on records collected after the mass radiography survey was completed. Hence the figure for all workers is slightly different from that shown in Table VII.)

† N.B.—A room may contain more than one department.

fewer workers per room and more space per worker in the rough-stuff departments than in any other occupational group. Hence the risk of droplet infection is relatively slight.

The occupational analysis as a whole indicates that the low incidence of active pulmonary tuberculosis among male rough-stuff workers was due to the fact that they were less exposed to infection than other men. It also suggests that the difference between these men and other boot and shoe operatives may be due, in the first instance, to selective recruitment.

Regional Analysis

In the first report it was shown that there was a statistically significant excess of newly discovered active cases of pulmonary tuberculosis in male boot and shoe workers in the Northampton, Kettering, and Rushden areas, but not in the Wellingborough area. As soon as the relationship between factory size and incidence of overt pulmonary tuberculosis was established, the apparently exceptional state of affairs in the Wellingborough area became understandable. Although this region includes the third largest town in the county, it has only one factory with more than 200 workers and none with more than 350. There were no other findings of special interest in the regional analysis.

Discussion

Hitherto, reports on the tuberculosis findings of mass radiography surveys have tended to concentrate attention upon newly discovered active cases and to ignore other types of disease (Ministry of Health Annual Reports, 1943–9; Clive, 1943; Brooks, 1944; Dick, 1945; Bradbury, 1947; etc.). Persons in need of treatment are undoubtedly of greater interest to clinicians than those in whom the disease is quiescent, but it is surely an overstatement to say that the incidence of healed lesions "is of no practical importance." In fact, an epidemiologist has as much—or more—to learn from the distribution of inactive and previously notified cases as from the distribution of active newly discovered cases.

At present there is no agreement between medical officers in charge of mass radiography units on what cases should be included in the inactive disease categories.* It is therefore inadvisable to compare one survey with another. On the other hand, the records of one observer can be used to discover what relationship, if any, the distribution of quiescent lesions bears to the distribution of active cases in different subgroups of the population examined.

Furthermore, while some mass radiography units invite all and sundry to avail themselves of the services provided (Medical Research Council, 1945; Dick, 1945; Maclean, 1947), others advertise the service as one which is not intended for those who are already under medical supervision (Bradbury, 1947). In any case, without special propaganda, known tuberculous subjects are less likely to attend than other persons. Provided, however, they were not deliberately excluded it might be possible to study the relative incidence of previously notified cases in different sections of a single community surveyed at one time, and to discover what proportion of these persons continue working in spite of having active disease.

The staff of mass radiography units are instructed to keep a careful record of the age, sex, and occupation of all persons examined. They are, however, rarely asked to obtain the same information about those who are not examined, even in clearly defined groups such as schools and factories. Unless, however, steps are taken at the time of the survey to establish the age, sex, and occupational constitution of the whole "population at risk," to discover which of the subjects have shared a common background and how many of their immediate colleagues have not been examined, it is impossible for the medical officer in charge to extract more than a limited amount of information from his records.

The present body of data is unique in more respects than one. In the first place, the original survey included approximately two-thirds of all workers in the staple industry of one county. This enabled Dr. C. M. Smith to identify more active undiagnosed cases in boot and shoe factories than elsewhere and to show that the excess was largely confined to three of the four departments in which there were a majority of male workers. A detailed study of the records of individual boot and shoe factories then showed that the incidence of active tuberculosis was a function of factory size. At this point it became evident that, even supposing all the patients had contracted their disease elsewhere, there must still be something in factory life, as such, which was determining the disease pattern. In order to discover what this obviously important factor was, a detailed study of working conditions was made.

Here again we were fortunate. Although there is a wide range in the size of factories in the boot and shoe industry in Northamptonshire, the internal working arrangements are very similar. In some factories all the operatives are housed in one or two large workshops, and in others there is a separate room for each of the six main operations. Every factory is, however, equipped with the same type of machinery. Even the position of the machines conforms to a standard pattern, and in

*In Ministry of Health returns from 23 mass radiography units (July–December, 1947), the incidence of all types of "quiescent pulmonary tuberculosis" ranged from 0.24 to 13.32% for males and 0.23 to 11.03% for females. The corresponding figures for "inactive post-primary" lesions were 0.11 and 1.84% for males and 0.22 and 2.64% for females.

†The making of boot and shoe machinery in this country is largely in the hands of one company, which not only hires its products to boot and shoe factories but also advises on the lay-out of their workshops.

each occupational group the proportion of male and female operatives tends to be constant. Finally, working arrangements are so static that two years after the completion of the mass radiography survey it was possible to reconstruct the original lay-out of the factories and identify the whole population at risk in terms of sex, occupation, and room distribution.

Armed with this additional information, we have been able to show that tuberculosis carriers constitute a danger to fellow workers, and that the distribution of the cases in boot and shoe factories is such as would be expected with any disease due to droplet infection. Certainly the incidence of overt pulmonary tuberculosis in any industry or occupational group is dependent first of all upon whether the nature of the work is such as to attract or repel tuberculous subjects; but once a number of these have been recruited the further spread of the disease depends upon whether working conditions foster or inhibit its transmission. Owing to the relatively small number of cases in each of the disease categories (newly discovered, previously notified, active, quiescent, and "open" tuberculosis) it is impossible to produce gilt-edged statistics in support of these suggestions. There is, however, strong presumptive evidence to suggest not only that "whatsoever a man soweth, that shall he also reap," but also that the seed so liberally scattered in boot and shoe factories "fell into good ground and brought forth fruit."

In view of these findings it is perhaps worth considering whether we are at present obtaining the maximum amount of value from mass radiography surveys. From a clinical point of view it is impossible to overrate a service which enables us to detect tuberculosis in the earliest stage of the disease, and in this respect it would be difficult to improve the work which is being done. On the other hand, the present investigation does suggest that the potential contribution of mass radiography surveys to epidemiology is not only neglected but actually hampered by preoccupation with matters of clinical interest.

There are several ways in which the Ministry of Health could help to correct this bias. In the first place, it should be possible to formulate a generally acceptable definition of "quiescent pulmonary tuberculosis." Since medical officers in charge of mass radiography units attend a special course of instruction before taking up their duties, it should not be difficult to ensure much greater uniformity of record-keeping than at present exists. Secondly, the Ministry could stress the importance of knowing the exact distribution and interrelationships of all types of tuberculosis, and encourage the inclusion of known tuberculous subjects in mass radiography surveys. Finally, attention might also be drawn to the importance of correlating medical and non-medical data, providing trained workers for collecting the latter, and directing some of the surveys towards more detailed environmental research.

Summary and Conclusions

An investigation is described in which mass radiography statistics have been used to study tuberculosis morbidity rates in different occupational groups in Northamptonshire during 1945–6.

The following findings (already reported elsewhere) are confirmed: (*a*) the incidence of newly discovered active disease in 1945–6 was higher in the boot and shoe factories than in other industries in Northamptonshire; (*b*) in the boot and shoe industry this type of case was found as often among men as among women, but in other occupations women were chiefly affected; and (*c*) the case incidence was higher in large than in small boot and shoe factories, and higher for clickers, lasters, and finishers than for rough-stuff workers.

New facts relating to the incidence of inactive tuberculous lesions, previously notified cases, cases with tubercle bacilli in the sputum, and three subdivisions of the newly discovered active cases (acute, subacute, and chronic) have also come to light.

From the distribution of newly discovered cases of quiescent tuberculosis, it is evident that in 1945–6 Northamptonshire boot and shoe factory operatives were more exposed to infection than workers in other occupations.

In the male section of the boot and shoe industry there were an exceptionally large number of previously notified cases, chronic undiagnosed cases, and acute undiagnosed cases. There were some "open" cases of tuberculosis in each of these disease categories, but these were mainly concentrated in the chronic undiagnosed group. Male rough-stuff workers (mostly sole-cutters) were an exception to the general rule and had relatively low rates for all types of tuberculosis.

Compared with other industries in which women were employed, the female section of the boot and shoe industry (closing- and shoe-rooms) included a large number of previously notified cases; but compared with industries in which men were employed these cases were infrequent and rarely showed signs of active disease. There were many acute undiagnosed cases among female workers, but relatively few chronic undiagnosed cases. In these respects there were no significant differences between female boot and shoe operatives and women in other occupations.

Acute undiagnosed cases usually occurred in association with chronic cases (previously notified and undiagnosed), and the proportion of acute to chronic disease steadily increased with increase in factory size.

An independent survey of the boot and shoe factories included in the mass radiography survey has revealed the following facts: (*a*) room size—that is, workers per room—is a function of factory size—that is, workers per factory; (*b*) workshops in large factories tend to be more congested than workshops in small factories; (*c*) in other respects the internal working arrangements are very similar in all factories; (*d*) with a few exceptions—notably sole-cutting—the operations performed in boot and shoe factories do not entail much physical exertion; and (*e*) there are fewer persons per room and more space per worker in the sole-cutting or rough-stuff departments than in any other department.

There is no evidence that leather dust, in moderate concentration, produces pneumoconiosis.

The final conclusion is that certain types of work suit the requirements of physically handicapped persons, and that in densely populated workshops the transmission of airborne diseases is facilitated. These two factors are responsible for there being more tuberculosis in boot and shoe factories than elsewhere. They do not, however, apply to sole-cutters, partly because their work is relatively heavy, and partly because they are more widely spaced than the other operatives.

In other departments the presence of carriers has led to further spread of the disease, in spite of the workers being relatively resistant to tuberculosis. This further spread is shown by the fact that examples of recently acquired disease were found most often in those factories which had the largest workshops, and in those departments which had the most chronic cases.

We have great pleasure in thanking Dr. M. C. Brough, Dr. W. T. Bermingham, and other members of the Northamptonshire Mass Radiography Unit for their kind co-operation. Our thanks are also due to Dr. C. M. Smith and other members of the Northamptonshire Steering Committee for initiating the investigation; to Dr. W. T. Russell for statistical advice; to Mr. W. E. C. Brooksbank and Miss Daphne Coulthard for

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ADDENDUM.—Two years after completing its first tour, the Northamptonshire Mass Radiography Unit went round the county again. The final results of this survey are not yet available, but a preliminary inspection of the records suggests that the incidence of newly discovered active pulmonary tuberculosis among male boot and shoe operatives is now no higher than among men in other occupations. The exact significance of this finding cannot be appreciated until it is known how many of these men were examined for the first time; how many were new entrants to the industry; what type of case was discovered; and what was the age distribution of the population examined. It is, however, likely that boot and shoe factories in Northamptonshire are already reaping the benefits of having had a thorough comb-out of chronic carriers during 1945–6.

HAEMOPHILIA ASSOCIATED WITH NORMAL COAGULATION TIME

BY

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Haemophilia is a condition which has attracted considerable interest, and the clinical and laboratory features of the typical syndrome are well recognized. The average case presents no difficulty in diagnosis and can be recognized with a high degree of certainty. The means by which this is accomplished are the family history, the clinical picture, and the laboratory findings.

Family History and Clinical Picture

Haemophilia is "an inherited tendency in males to bleed" (Bulloch and Fildes, 1911). It is transmitted by apparently unaffected females. No other haemorrhagic diathesis with this type of inheritance has yet been described. The absence of such a history need not exclude the diagnosis, as apparently sporadic cases are not uncommon: they accounted for 39% of cases met with in one series (Merskey, 1950b).

The chief symptom is severe and often almost uncontrollable haemorrhage from even minor injuries. These haemorrhages may occur from skin and mucous membranes, into muscles and especially into joints. It is a severely disabling condition, the patients being constantly exposed to the risk of haemorrhage and often being crippled by the ankylosis of joints which so constantly follows the repeated haemarthroses. Very few haemophiliacs are able to lead normal lives, and the mortality rate in childhood and adolescence is considerable.

*Cecil John Adams Travelling Scholar, 1949.

Laboratory Findings

The bleeding time, platelet count, tourniquet test, and plasma prothrombin, factor V, and fibrinogen are all normal. On the other hand, the coagulation time is prolonged and prothrombin is not adequately consumed during coagulation of the blood.

The lengthening of the coagulation time of the blood is the best-known laboratory abnormality of haemophilia. Conflicting views have been expressed about whether a normal coagulation time can occur in haemophilia. Davidson *et al.* (1949) stated that they had never seen it. Birch (1937) stated that in mild haemophilia it might be normal at intervals, and Whitby and Britton (1946) that it might be almost normal between the attacks of bleeding. Quick (1949) reported a series of 24 haemophiliacs, 7 of whom had a Lee and White coagulation time of under 10 minutes, and he commented that in mild haemophilia the coagulation time could be normal; a similar statement was made by Tocantins (1949).

Brinkhous (1939) was the first to demonstrate defective consumption of prothrombin during coagulation of haemophilic blood, and this has since been confirmed (Quick, 1947; Soulier, 1948; Alexander and de Vries, 1949; Merskey, 1950a). By comparing the amount of prothrombin in the plasma with that present in the serum of blood clotted in glass tubes the amount of prothrombin "consumed" during coagulation can be measured. Normally, most of the prothrombin is converted to thrombin and very little remains in the serum. In haemophilia the serum often contains as much as the plasma and, for reasons not at present fully explained, in many cases apparently even more.

Patek and Stetson (1936) showed that there was a substance present in normal blood which was absent or unavailable in haemophilic blood. This substance, sometimes called antihaemophilic globulin, when added in small proportion to haemophilic blood shortened the coagulation time of the latter and also improved its prothrombin consumption defect (Quick, 1947; Soulier, 1948; Alexander and de Vries, 1949; Merskey, 1950a).

The absence of antihaemophilic globulin in haemophilic blood can be used as a diagnostic test for this condition. This can be demonstrated by adding to known haemophilic blood minimal proportions of the blood of a patient suspected of having haemophilia. If the suspected blood proves incapable of correcting the coagulation time and prothrombin consumption defect, the patient probably has haemophilia. If it can correct these defects of haemophilic blood to some extent, but not to that produced by an equal proportion of normal blood, it is probable that the patient has the haemophilic defect, but in less degree.

By the use of this test in a large series of haemophilic patients I was able to show (Merskey, 1950b) that varying grades of the haemophilic defect did exist. At the one extreme there were the classical haemophiliacs with prolonged coagulation time, grossly defective prothrombin consumption, and inability to correct haemophilic blood; at the other extreme patients with normal coagulation time, a much milder prothrombin consumption defect (in some instances no demonstrable defect at

all), and a partial ability to correct haemophilic blood. Between the two extremes all grades of these defects were found.

It is the purpose of this paper to describe the clinical features of patients in whom the coagulation time was normal or near normal, and whose blood possessed some ability to correct the defects of known haemophilic blood. In no instance was this ability equal to that of normal blood. In the series of 54 patients (Merskey, 1950b) the coagulation time was greatly prolonged in 33, slightly prolonged in 12, and not at all prolonged in 9. The patients to be described belong to the second and third groups.

Case Histories

The family trees in each of the eight families are shown (Figs. 1–8). An analysis of main symptoms in available cases is shown in Table I, and the laboratory findings are summarized in Tables II and III.

Fig 9 demonstrates the relative inability of the plasma of patients IV 5 of family 1 and IV 6 of family 3 to correct that of a haemophiliac with prolonged coagulation time. Fig. 10 shows the same phenomenon with regard to patient IV 16 of family 4, while that for IV 3 of family 5 is shown in Fig. 11. This test was carried out on the blood of at least one member of each of these eight families.

Family 1

The inheritance of the disease in this family follows the classical course, and at least seven members show symptoms of haemophilia (Fig. 1).

III 7 and III 8 are affected in much the same way. Cuts and scratches usually bleed little more than normal. Occasionally haemorrhage is troublesome. They both bruise easily and have considerable haemorrhage after dental extraction, when they may bleed for two to three weeks. The elder has had no joints involved, but the younger has had swelling of one ankle, which occurred after only mild trauma, and swelling of the knee-joint following a severe injury.

IV 4, 5, 6, and 7 are all affected in the same way, though IV 6 is even less affected than the others. All except IV 6 have had at least one severe bleeding episode which continued for days. These episodes usually followed injuries to lips or tongue. Generally cuts have bled little if at all more than would be expected in a normal person, and haemorrhagic episodes of any degree were separated by years. Small bruises were common, and occasional large bruises after injuries have taken weeks to subside. In all four patients haemorrhage occurred when the milk teeth were lost, and considerable bleeding followed tooth extraction. All have had one, and at most two, episodes of haemarthrosis, though with one exception these followed quite severe trauma. The only apparently spontaneous haemarthrosis was in IV 5, who twice had a swollen hip-joint without obvious injury. IV 4 has a little residual ankylosis of a knee-joint; also he once vomited some blood and had a melaena stool following a "heavy fall." IV 7 once fell off a bicycle and bled intraperitoneally, requiring blood transfusion. They have all had frequent epistaxis, but none has had haematuria.

TABLE I.—*Analysis of Main Symptoms in all Available Cases*

Family	No.	Year of Birth	Severity of Bleeding		Bruises	Epistaxis	Bleeding After Dental Extractions	Haemarthroses			Gastro-intestinal Haemorrhage	Haematuria	Personal Interrogation
			Usual	Occasional				No. of Joints Involved	Following Obvious Injury	Residual Ankylosis			
1	III 7	1895	Normal	Excessive	Frequent	?	Severe	0	—	—	Nil	Nil	No
	III 8	1908	,,	,,	,,	?	,,	2	No	Nil	,,	,,	,,
	IV 4	1925	,,	,,	,,	Frequent	,,	1	Yes	Slight	Once after injury	,,	Yes
	IV 5	1930	,,	,,	,,	,,	,,	1	No	Nil	Nil	,,	,,
	IV 6	1930	,,	Normal	,,	,,	,,	1	Yes	,,	,,	,,	,,
	IV 7	1930	,,	Excessive	,,	,,	,,	1	,,	,,	,,	,,	,,
2	I 1	?	?	,,	?	,,	?	0	—	—	?	Occasional	No
	III 7	1912	Normal	,,	Frequent	,,	Severe	2	No	Nil	Once	Nil	Yes
	III 8	?	,,	,,	?	Nil	?	0	—	—	?	?	No
	IV 1	1939	?	?	?	?	?	?	?	?	?	?	?
	IV 3	1944	Normal	,,	Frequent	Frequent	?	1	Yes	?	?	?	,,
3	IV 6	1933	,,	,,	Nil	,,	Severe	1	,,	No	Nil	Nil	Yes
4	III 19	1908	,,	,,	Frequent	,,	,,	0	—	—	,,	,,	No
	IV 14	1930	,,	,,	,,	Nil	,,	0	—	—	,,	,,	,,
	IV 16	1937	,,	,,	,,	Frequent	,,	0	—	—	,,	,,	Yes
5	IV 3	1932	,,	,,	,,	,,	,,	4	No	Nil	,,	,,	,,
6	V 4	1913	,,	,,	,,	,,	,,	Multiple	,,	Yes	Frequent	Frequent	,,
7	III 5	Died aged 45	,,	,,	,,	Occasional	,,	4	,,	Nil	,,	Nil	No
	III 6	Died aged 23	,,	,,	,,	,,	—	4	,,	,,	,,	,,	,,
	III 7	1911	,,	,,	,,	,,	Severe	4	,,	Yes	Nil	,,	,,
	III 8	1914	,,	,,	,,	,,	,,	1	Yes	Nil	Frequent	,,	Yes
8	IV 30	1921	,,	,,	,,	,,	,,	2	No	,,	Nil	Once	,,
	IV 32	1926	,,	,,	,,	Frequent	,,	2	Yes	,,	,,	Nil	,,
	IV 17	1939	,,	,,	,,	,,	,,	4	No	Slight	,,	,,	,,
	IV 12	1946	,,	,,	,,	,,	—	1	,,	Nil	,,	,,	,,

TABLE II.—*Blood Coagulation Times and Interpretation as Reported by Other Observers*

Family	Patient	Year	Coagulation Time (Seconds)	Method	Interpretation
1	IV 4	1928	207	Dale & Laidlaw	Prolonged
		1938	180	,, ,,	,,
	IV 5	1932	220	,, ,,	,,
	IV 7	1935	220	,, ,,	,,
		1938	170	,, ,,	,,
2	IV 1	1941	155	?	Slightly prolonged
		1943	180	?	Raised
	IV 3	1949	—	—	Normal
4	III 19	1950	450	"Capillary"	Slightly prolonged
5	IV 3	1936	—	—	Normal
		1946	200	?	,,
		1946	330	Dale & Laidlaw	,, (!)
6	III 8	1949	—	—	Normal
8	IV 12	1947	660	Dale & Laidlaw	Prolonged

TABLE III.—*Laboratory Findings Observed at Radcliffe Infirmary*

Family	Patient	Date	Coagulation Time and Method Used				Prothrombin Consumption Index %		
			Lee & White	Dale & Laidlaw	Quick's Test (Seconds)		Source of Serum		
			(Individual Tubes) (in Minutes)	(Seconds)	Slow Spun	Fast Spun	Whole Uncitrated Blood		Citrated Plasma Recalcified
							Venous	Capillary	
1	IV 4	Nov., 1949	9½, 9½, 9½, 11	205	—	—	60	12	25
		1948	9½, 10, 11½, 23	—	—	—	—	—	—
	IV 5	Nov., 1949	8, 8½, 9, 11½	200	—	—	47	<5	75
		Jan., 1950	9, 10½, 10½, 12	—	258	547	—	—	—
	IV 6	Nov., 1949	7½, 8, 8, 8	135	—	—	27	5	20
	IV 7	March, 1950	9½, 9½, 9½, 11	205	—	—	60	12	25
2	III 7	April, 1949	7½, 8, 8, 8	135	—	—	133	—	—
		Nov., 1949	8, 8, 8½, 9	165	—	—	115	<5	<5
		Feb., 1950	9½, 7½, 12, 8	165	172	347	90	—	26
3	IV 6	June, 1949	4½, 9, 6½, 8½	—	—	—	24	—	—
		Nov., 1949	7½, 8, 8, 8	152	—	—	41	12	—
		March, 1950	7½, 7½, 7, 7½	185	204	270	19	<5	13
4	IV 16	Feb., 1950	9½, 9½, 9½, 10½	190	225	430	36	<5	45
5	IV 3	Dec., 1946	12½, 12½, 13, 12½	200	—	—	—	—	—
		May, 1949	8½, 8½, 8½, 14½	125	—	—	88	—	32
		Nov., 1949	5½, 7½, 7½, 8	153	—	—	74	<5	7
		Jan., 1950	9, 9½, 9½, 9½	155	187	250	—	—	—
6	V 4	March, 1942	13½	—	165	225	—	—	—
		Feb., 1946	7½, 8, 8, 9½	—	—	—	—	—	—
		Aug., 1949	7, 7, 6½, 9	155	—	—	65	—	—
		Aug., 1949	6½, 6½, 6½, 7	—	—	—	75	—	—
		March, 1950	5, 6, 6, 5	105	166	296	86	10	43
		April, 1950	12, 12½, 13½, 15	—	—	—	—	—	—
7	III 8	Jan., 1950	12½, 13½, 13½, 13½	—	—	—	—	—	—
		Jan., 1950	14, 15½, 13, 15½	160	259	353	94	<5	115
		Feb., 1950	9, 11½, 14, 14	—	—	—	—	—	—
8	IV 12	Nov., 1947	11½, 13, 26, 46	—	214	364	—	—	—
		Nov., 1949	6, 6, 7	255	222	290	113	16	100
	IV 17	April, 1949	9, 10, 10½	170	—	—	44	—	—
		Nov., 1949	10½, 11, 10½, 14½	318	—	—	48	6	80
	IV 30	March, 1950	10½, 12, 12, 12	230	274	500	74	<5	31
	IV 32	March, 1950	11½, 12, 12, 11	260	—	—	83	<5	43

Family 2

The inheritance of the disease in this family is classical, and at least five members appear to be affected (Fig. 2).

I 1 had epistaxis, haematuria, and severe bleeding from cuts, but no joint lesions. He died at the age of 87.

III 7 hardly bleeds at all from small cuts, but on occasion larger cuts have bled for hours. He once bled for a month after extraction of four teeth, and on another occasion haematemesis and melaena were severe enough to warrant urgent blood transfusion. He has had two episodes of haemarthrosis (knee and metatarso-phalangeal joint). He bruises easily and has frequent epistaxis.

III 8 bled severely from tooth extraction and also from cuts. He bruised easily but had no swollen joints or epistaxis. During military service he was accidentally shot in the pelvis and died a week later, supposedly from haemorrhage.

IV 1 had two episodes of severe haemorrhage following cuts on lip and tongue. He died at the age of 6 from a "fractured neck."

IV 3 bruises easily and has much epistaxis. On one occasion he had a swollen ankle-joint, and he once bled so severely from a cut lip that he required blood transfusion.

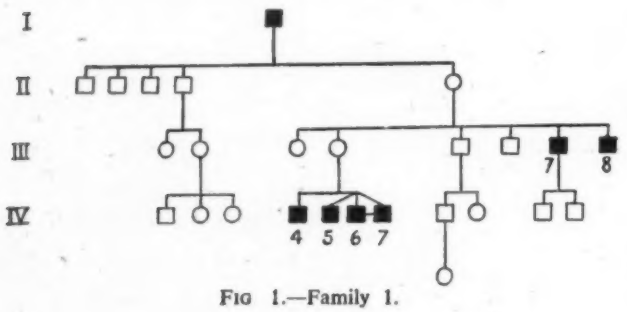

FIG 1.—Family 1.

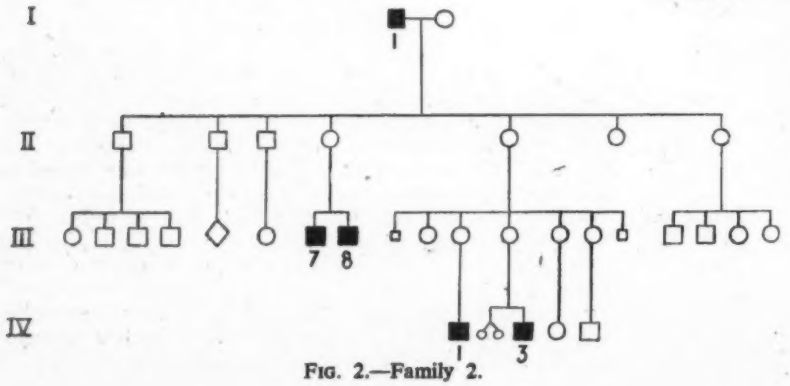

FIG. 2.—Family 2.

Family 3

Apart from a very doubtful history of bleeding in the second generation there is no family history of haemorrhage (Fig. 3).

II 4 bled severely after tooth extraction and once after injury, but not after severe war wounds.

II 15 had epistaxis on several occasions.

IV 6 bled severely after circumcision and from minor cuts and scratches. He has had repeated epistaxis and bled severely after loss of milk teeth and on extraction of others. On one occasion, after being knocked down by a bicycle, a knee-joint became swollen, but this soon subsided. There is one spider naevus on the left side of his nose.

Family 4

The inheritance in this family is once again classical for haemophilia, at least 10 members being affected (Fig. 4).

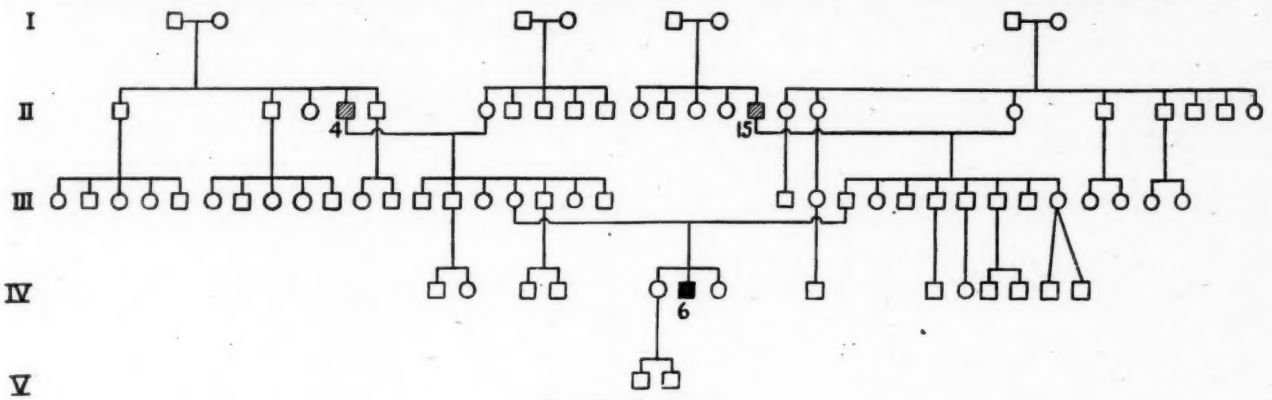

FIG. 3.—Family 3.

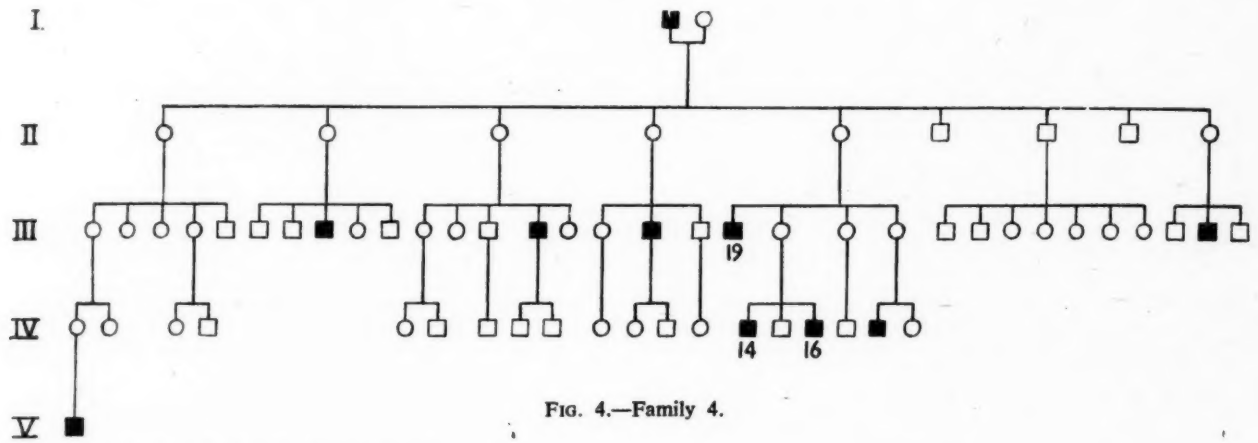

FIG. 4.—Family 4.

IV 14 bruised easily but had no epistaxis, haematuria, gastro-intestinal bleeding, or swollen joints. Tooth extractions bled for one month despite blood transfusion. He died at the age of 5½ after tonsillectomy. Haemostasis had been secured at operation, but fatal bleeding began seven days later.

III 19 and IV 16 have similar histories. Cuts have often bled very little, but on a number of occasions haemorrhage has continued for weeks. Bleeding for two to three weeks has also followed tooth extraction, while epistaxis has been frequent and severe. They bruise very easily. IV 16 plays cricket and soccer for his school team. III 19 has been an epileptic since the age of 7.

Family 5

It has been possible to trace only one affected member in this family (Fig. 5).

IV 3 bled severely after circumcision. He has also bled for weeks after biting his tongue or cutting his finger or lip and after dental extraction. On a number of occasions his life was saved only by urgent blood transfusion. He has always bruised easily, has had repeated epistaxis, and both ankles and both shoulder-joints have become swollen and painful. These swellings have subsided after a few weeks and left no residual deformity.

Family 6

There is one apparent discrepancy in this large and otherwise typical family history of haemophilia, as III 9 is stated to have been normal (Fig. 6).

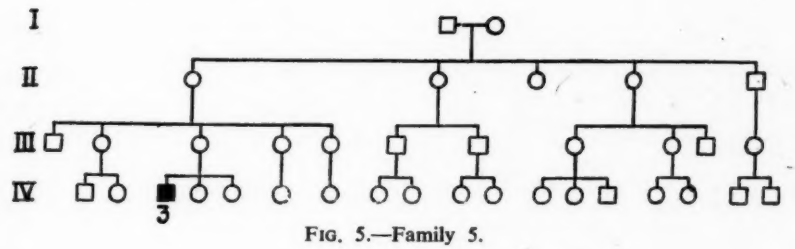

FIG. 5.—Family 5.

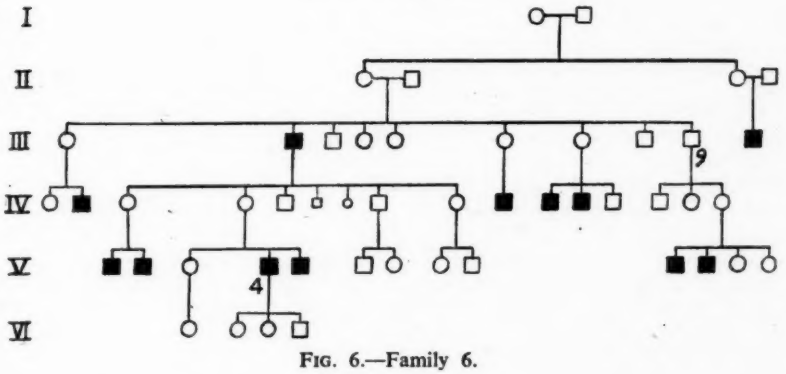

FIG. 6.—Family 6.

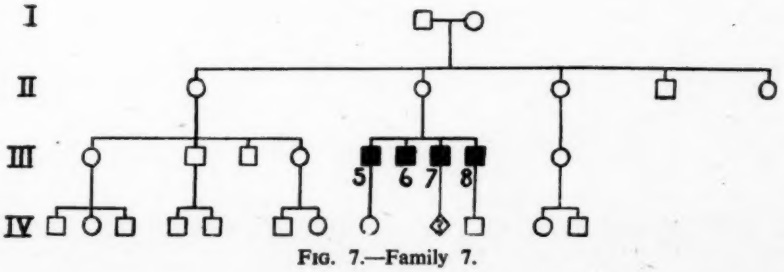

FIG. 7.—Family 7.

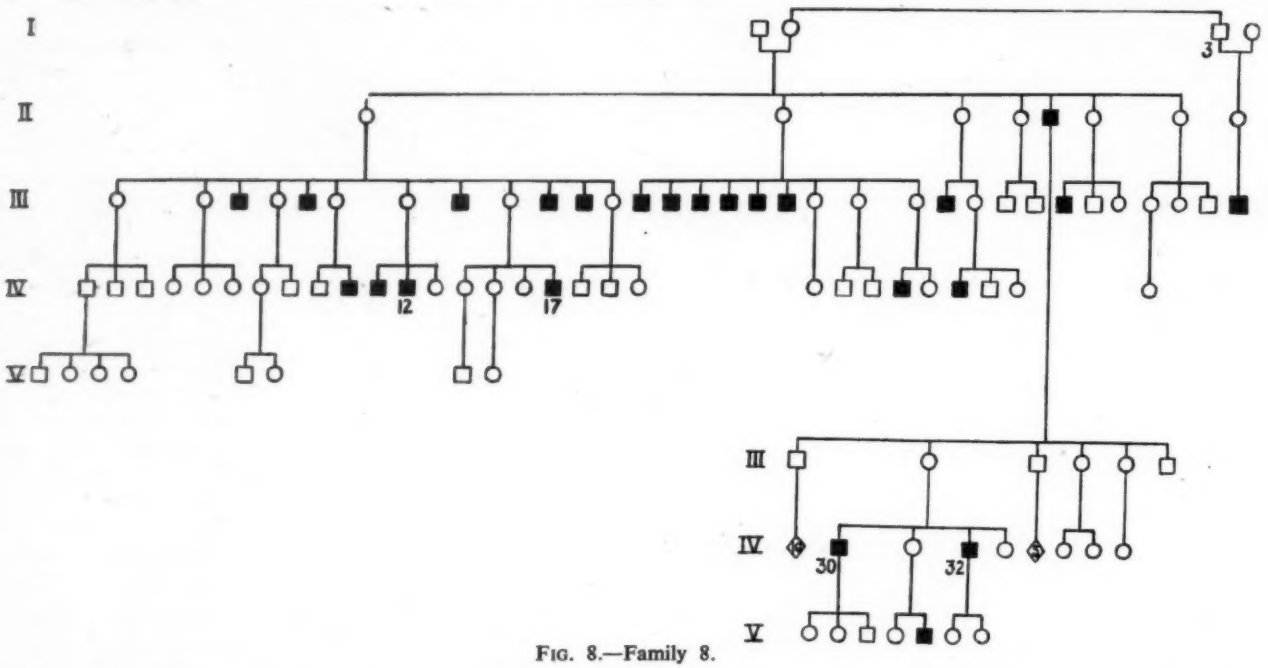

FIG. 8.—Family 8.

V 4 has been a bleeder since infancy, when he was reputed to have bled from the bowel. He has had a great number of hospital admissions for haemorrhagic episodes. Cuts have occasionally bled for hours or days; he has had severe bruising and enormous intramuscular haematomata, multiple haemarthroses with resulting joint deformity, prolonged epistaxis, and many episodes of melaena and haematemesis. He has bled for weeks or months after dental extraction. Numerous barium-meal examinations of stomach and duodenum failed to reveal an ulcer, but on the last occasion he was said to have a deformed duodenal cap. He has a history of indigestion compatible with a peptic ulcer.

This case demonstrates how a severe clinical syndrome may occur in the presence of a normal coagulation time.

Family 7

Apart from the four affected brothers no other case has been discovered in this family (Fig. 7).

III 5, 6, and 8 all had similar histories. They all bruised very easily, but cuts hardly bled more than normally except on rare occasions, when the bleeding was severe. The first two had painful swellings of knees and ankles after mild injury; the third brother developed a joint swelling on one occasion and then only after a severe knock with a cricket ball. III 6 had never had a tooth extracted, but the other two had bled for up to 48 hours after an extraction. But the chief symptoms of these three subjects was severe and repeated haematemesis and melaena. None had ever had indigestion and no peptic ulceration could be demonstrated on barium-meal *x*-ray examination. The two eldest brothers had died of gastro-intestinal haemorrhage even after multiple blood transfusions. Necropsy on one disclosed "multiple petechial haemorrhages of stomach and three superficial erosions in the duodenum, but no other pathology."

The fourth brother, III 7, has a similar history as regards cuts, bruises, and tooth extraction, but has never had gastro-intestinal haemorrhage. Instead he has had repeated haemarthroses, the knees and elbows especially being involved, and several joints have restricted mobility.

The history of bleeding in this family is somewhat atypical, as there seems to be a special tendency for gastro-intestinal bleeding.

Family 8

This very large family shows classical inheritance except for I 3, who is said to have been normal (Fig. 8).

IV 12 had no symptoms until the age of 15 months, when he was admitted to the Radcliffe Infirmary because of a haemorrhage into the spinal canal (Schiller, Neligan, and Budtz-Olsen, 1948). He has since bled severely from a cut lip and has had repeated haemorrhages into one ankle-joint.

IV 17, 30, and 32 all have similar histories. They have bled excessively after cuts and on occasion have needed transfusion. Some cuts bled very little. They all bruise easily and have had repeated epistaxis. Tooth extractions have bled for weeks and on occasion required many blood transfusions. They all had repeated haemarthroses, but the swellings have often not lasted more than a week. There was 10 degrees limitation of flexion of the right knee in IV 17, but, apart from this, all joints were freely mobile. IV 30 had one episode of haematuria.

This family demonstrates that the same grade of haemophilia can occur in widely separated branches of the same family.

Full physical examination carried out on the subjects in all of the families failed to reveal other significant abnormalities. A special search was made for capillary telangiectasia.

Laboratory Findings (Tables II and III)

The bleeding time, tourniquet test, platelet count, and plasma prothrombin were found to be within normal limits.

Coagulation Time of Whole Blood

The cases described here were selected because of their normal or near normal Lee and White coagulation time. In this laboratory we regard 11 minutes for the Lee and White test and 180 seconds for the Dale and Laidlaw technique as being outside the normal range (Merskey, 1950b). On these standards the readings encountered in the patients in this series (Table III) were usually, but not invariably, normal. Slight fluctuations above and below the normal range occurred. The readings in family 7 were always outside the normal range in the Lee and White test, while those in family 8 also tended to be in excess of normal. Occasionally, especially in family 1, the Dale and Laidlaw readings were abnormal when Lee and White readings were normal or only on the borderline of abnormality.

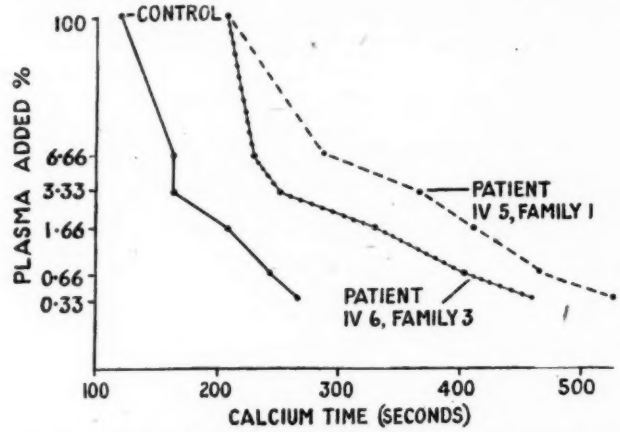

FIG. 9.—Shortening of calcium time of known haemophilic plasma produced by blood of patients IV 5 of family 1 and IV 6 of family 3 as compared with that of a normal control. Note the relative inability of the patients' blood to correct the known haemophilic blood. The percentage of plasma added is plotted on a logarithmic scale. The calcium time of the haemophilic plasma alone was 765 seconds.

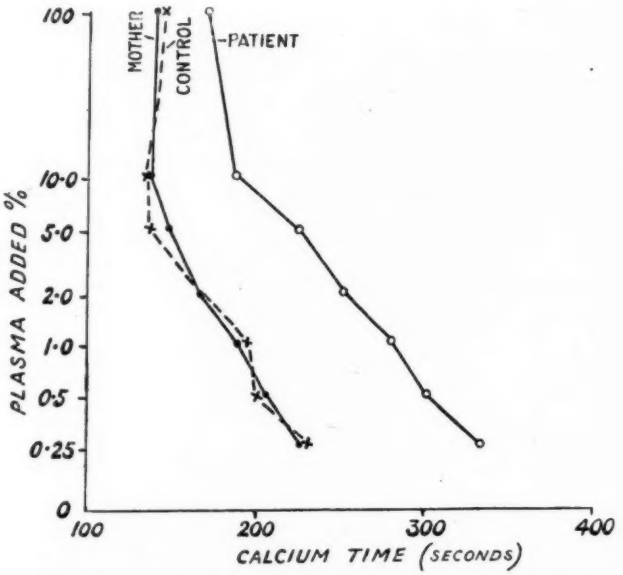

FIG. 10.—As for Fig. 9. Patient IV 16 of family 4, a normal control, and the mother of the patient. The calcium time of the haemophilic plasma alone was 502 seconds.

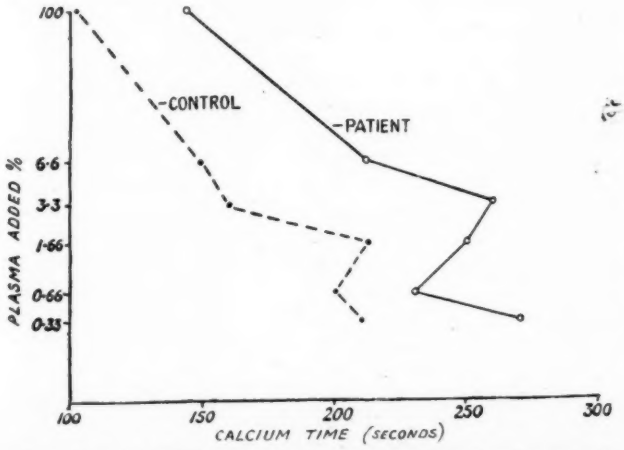

FIG. 11.—As for Fig. 9. Patient IV 3 of family 5 and a normal control. The calcium time of the haemophilic plasma alone was 287 seconds.

The readings remained relatively constant over prolonged periods, and the short coagulation times were not due to a fluctuation of a prolonged coagulation time towards the normal range (Tables II and III). Many patients stated that their blood tests had always been found to be normal. There seemed little doubt that the normal coagulation time was a constant feature.

Quick's test for haemophilia measures the increase in the calcium clotting time produced by centrifuging oxalate plasma to precipitate platelets. Quick (1941) claimed that this increase was much greater in haemophilic than in normal plasma. Since the calcium time of normal oxalate plasma may, on occasion, be increased by 100%, Quick's test will be significant only if the increase exceeds this figure. Such increases occurred in only two out of nine tests performed in this series. The test was therefore of little value in the diagnosis of these cases. Similar results were obtained in cases of haemophilia with prolonged coagulation time (Merskey, 1950b).

Prothrombin Consumption Index

With serum from whole clotted venous blood or recalcified citrate plasma the normal range for this test is always under 40% and often under 20% (Merskey, 1950a). In the 14 patients of this series this test gave abnormal readings in 11 instances, while 3 came into the normal range. In the usual case of haemophilia with prolonged coagulation time values of over 100% and even up to 200% are commonly encountered, but such readings were only exceptionally seen in this series. When the test was done on the serum from clotted capillary (finger-prick) blood normal results were obtained in all cases.

Titration of Antihaemophilic Globulin

This test was carried out on the blood of at least one member of each of these families, and the result showed a deficiency of this substance when compared with a normal control. From the fact that these patients could improve to some extent the defects of known haemophilic blood it seemed likely that they had less of the haemophilic defect and possibly more available antihaemophilic globulin than did cases of haemophilia with prolonged coagulation time. This test was used as the final test in doubtful cases.

Discussion

In these patients the clinical symptoms varied in degree from mild to severe, but remained relatively constant in any particular family. Patients in families 1 to 5 had a mild clinical syndrome, those in family 8 were a little more severely affected, while those in families 6 and 7 were severely incapacitated. Where the syndrome was mild and crippling haemarthroses were absent the patients were able to lead relatively normal lives. One of the adults worked as a lorry driver, and several of the younger patients engaged in strenuous sports.

The symptoms were those of classical haemophilia, but the haemorrhagic episodes were often widely separated. Small wounds as a rule gave very little trouble, and cuts and scratches bled no more than would be expected in normal individuals. Yet most of the patients had had at least one severe bleeding episode requiring urgent blood transfusion and even seeming to threaten life. Dental extractions were especially troublesome, severe bleeding often continuing for days or weeks. One patient died after tonsillectomy and another bled for many weeks after laminectomy

and required in all 63 blood transfusions to control haemorrhage (Schiller, Neligan, and Budtz-Olsen, 1948). It is possible that surgery is safer in this type of haemophilia than in the type with prolonged coagulation time, but, even so, the risk of haemorrhage is formidable.

Epistaxis and easy bruising were practically invariable. The latter symptom is uncommon in normal males, and more than one intelligent mother in a haemophilic family had diagnosed haemophilia in her infant son on this symptom alone. If the trauma was severe enormous bruises might be produced.

Haemarthroses were infrequent, and this fact provided a very striking difference between this syndrome and that of haemophilia with prolonged coagulation time. If they did occur they were only rarely apparently spontaneous and usually followed severe injury. Frequently only one joint was involved, and the swellings might last for only a week or two and leave slight deformities. As a result most of the adults were not incapacitated by ankylosed joints and were thus able to follow relatively normal lives.

Inheritance.—In the six families in which there was a familial history this closely resembled the classical inheritance of haemophilia, there being only two apparent discrepancies (family 6, III 9; family 8, I 3). Both these patients were alleged to be normal.

The various members and generations of the same families all seemed to have the same type of clinical picture and degree of laboratory abnormality. The syndrome thus appeared to breed true.

The importance of the recognition that haemophilia can occur with a normal coagulation time cannot be overstressed. Many of these patients had been told that surgery could safely be undertaken, and it was only after alarming haemorrhage had occurred that it was realized that the advice given had been incorrect. These patients must be regarded as haemophiliacs with all the serious implications of that diagnosis.

There are only very scanty references to this syndrome in the literature. The references to haemophilia with normal coagulation time cited earlier also mention a milder syndrome of haemophilia (Birch, 1937; Quick, 1949; Tocantins, 1949). Fowler (1949) stated that some cases of haemophilia are mild, while Sköld (1944) described some cases of haemophilia with normal coagulation time and without haemarthroses. Some of his cases had a normal coagulation time and a mild syndrome, while others in the same family had a prolonged coagulation time and a more severe syndrome. The only extensive papers on this syndrome are those of Davenport (1930) and Haldane (1935), both of which discuss some haemophilic families in whom the clinical picture appeared to be mild. Unfortunately laboratory data are too scanty to be of value.

Summary

The pathology of haemophilia is reviewed. It is pointed out that the disease occurs in varying grades of severity as estimated both clinically and in the laboratory.

Cases occurring in eight families are described in detail because, as part of a larger survey, they were all found to have normal coagulation times, and the other commonly practised blood tests were also normal in the majority of instances. The bloods of these patients were poor at shortening the calcium time and correcting the prothrombin-consumption-defect of known haemophilic blood, however, and clinically there was no doubt whatsoever that these people had haemophilia.

Attention is drawn to the danger of relying on the common bleeding and clotting tests to exclude the possibility of haemophilia.

My thanks are due to Dr. A. H. T. Robb-Smith, Director of Pathology, Radcliffe Infirmary, and Dr. R. G. Macfarlane, in whose department this study was carried out; to Professor L. J. Witts for facilities in his department; to Dr. R. G. Macfarlane and Dr. Rosemary Biggs for constant advice and encouragement; and to Miss J. Lee and Miss J. Lash for technical assistance. The expenses of this investigation were defrayed by the Nuffield Foundation Haematology Research Fund and the Medical Research Council.

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THE MYRMECIA

A STUDY OF INCLUSION BODIES IN WARTS

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[WITH SPECIAL PLATE]

The infective nature of warts was first convincingly demonstrated by Jadassohn (1896), who had 33 positive inoculations out of 86 attempted. Ciuffo (1907) found that the infectious agent present in ground wart tissue would pass Berkefeld N, and Serra (1908), Wile and Kingery (1919), and Kingery (1921) Berkefeld W filters. Passage of experimentally produced warts to the second generation was achieved by Tuccio and Coppolino (1912), Kingery (1921), and Ullmann (1923–4). The elementary bodies of human wart virus have never been described, and the evidence for the viral aetiology of warts rests upon the above experiments.

Histological Appearances

On the assumption that warts were due to a virus we looked for inclusion bodies in sections of warts taken from a pilot series of 10 cases. The wart tissue was curetted under local analgesia, and was fixed in formol-Zenker and stained with haematoxylin and eosin. We found that five of the patient's warts contained eosinophilic intranuclear and intracytoplasmic bodies in the prickle-cell layer (Plate, Fig. 1), and in the belief that these were inclusion bodies we named these warts type I, for "inclusion." Warts from the remaining five

patients were devoid of these eosinophilic bodies, and such warts we named type B, for "banal," on account of their commonplace histology.

The most obvious change in the type I wart when seen under the low-power microscope was a gross disorder of the architecture of the prickle-cell layer. The bodies which we found in type I warts were eosinophilic. Those bodies which were intracytoplasmic could be found in the whole depth of the prickle-cell layer. In the cytoplasm of the deepest layer of prickle cells, and also in an occasional basal cell, we could detect minute pink granules (Fig. 2), which in the succeeding layers of cells increased in size and number. Clear spaces soon appeared within the bodies (Fig. 3) and resulted in rings and sickles and other bizarre shapes. The bodies looked as though they were made of red paraffin wax, and this impression was heightened by their apparent fusion in the upper parts of the prickle-cell layer, where they formed large eosinophilic masses surrounding the nucleus (Fig. 6).

As in molluscum contagiosum, not all the prickle cells were involved in the process, and those cells which escaped were compressed between those which were involved. Those deep prickle cells which were affected differed from those which escaped only in the possession of the minute eosinophilic intracytoplasmic bodies, and in particular the prickles of the affected cells were intact. But in the middle layers of the stratum spinosum the affected cells were much swollen, and their nuclei were large and pale. In the nuclei of some of the affected cells there developed intranuclear eosinophilic inclusion bodies which were perfectly round, and which were bordered by a pale halo (Fig. 4). Such inclusions correspond with intranuclear inclusions type B of Cowdry (1934): these type B inclusions must not be confused with the type B warts of this paper.

At the level of the stratum granulosum the intracytoplasmic inclusion bodies became fewer and larger, and clothed the nucleus. The nuclear substance changed, first from a translucent to a ground-glass appearance (Figs. 4–6), and then became basophilic. The intranuclear inclusions disappeared at this level.

In the stratum corneum the nuclei of the affected cells persisted for a time, became deeply basophilic (Fig. 7), and then shrank and split or fragmented (Fig. 8), until finally they and the fused masses of the intracytoplasmic inclusions became extensively vacuolated (Figs. 9 and 10).

The whole substance of the wart was not uniformly involved by the process; the central part was more affected than the peripheral, and portions of individual papillae were spared. The unaffected parts of the stratum spinosum were seen to underlie those areas of the horny layer which were devoid of nuclei.

There is a close similarity between the histology of molluscum contagiosum and that of type I warts. In molluscum contagiosum there is the same involvement of some of the prickle cells, and the altered cells can be traced from the bottom of the prickle-cell or even the basal-cell layer. The development of the inclusion (molluscum) bodies can be followed through the successive epidermal layers; between the affected cells can be seen the squeezed remnants of those which have escaped. There are two main differences between the diseases: in molluscum contagiosum the nuclei of the affected cells are displaced by the developing inclusion bodies, whereas in type I warts the nuclei remain central, and there are no wart bodies produced comparable to the molluscum bodies.

The staining reactions of the bodies in type I warts are those which would be expected of inclusion bodies. Thus they stain with Mann's, Laidlaw's, and Downie's stains, but not by the Feulgen technique or by the Prussian-blue reaction for iron. With Feulgen's stain the intranuclear inclusion bodies show up as pale areas within the nuclei in contrast with the nucleoli, which are dark. We were unsuccessful with the phloxine-tartrazine stain, but Lendrum (1947) illustrates a type I wart in his paper on this stain.

Clinical Appearances

After establishing the existence in warts of bodies compatible with inclusions we examined a larger series of cases. The warts from 102 consecutive patients were examined microscopically with the same method of fixation and staining as before. Their warts were type B in 62 cases, type I in 36, and of an intermediate type in 3. The remaining patient had a lesion which was histologically a granuloma pyogenicum, and he was excluded.

The type I warts were mostly plantar, palmar, subungual, or on the pulp of a digit, whereas the type B warts were predominantly common warts of the fingers, face, scalp, and knees. A clinical diagnosis of the expected histological type was eventually possible and, apart from the site of the warts, depended on the following features. Pain, redness, and swelling were commonly associated with type I warts, and in some cases had led to the diagnosis of a whitlow; no pus was found macroscopically or microscopically. Symptoms and signs of inflammation in type B warts were invariably associated with obvious pus formation.

The type I warts were deeply set in the skin, and could be compared to an iceberg floating in water, in contrast with type B warts, which were set superficially, like a cork floating on the surface. As a result the type I warts looked like little molehills with domed tops, while the type B ones were typical warty excrescences. Type I warts might be completely covered by the horny layer, especially on the soles of the feet, but as a rule the horny layer was incomplete over their crowns and formed a thick hyperkeratotic collar; until this collar was removed the full extent of the underlying wart tissue could not be appreciated. Consequently type I warts lay in a flask-shaped cavity, wider at the bottom than the top, while type B warts lay in a saucer-shaped depression.

Type I warts were single individuals, and their cavities were therefore circular in outline. When more than one type I wart inhabited a piece of skin the cavities remained distinct, and there was never the aggregation of many warts into a plaque which was sometimes seen in type B warts: removal of such a plaque would leave a cavity with a polycyclic border. After curettage the type I warts were bulkier than type B, and softer and more resilient to feel; their white opaque bodies and yellowish somewhat friable crowns were of approximately equal thickness, as compared with the tough, horny crowns of type B warts, which were much thicker than and often overshadowed their compact bodies.

The impression conveyed by curetting a type I wart was of plunging the curette into a hole and scraping until suddenly the soft white wart tissue exuded, often in fasciculi like a shallot; type B warts simply needed to be scraped off the skin. The seedlings surrounding type I

warts were set in the skin like sago grains, for the horny layer covered them completely; those surrounding type B warts were on the skin, for the horny layer was interrupted by their presence, and therefore they had a rough surface.

The series revealed other clinical differences. Thus type I warts had usually been present for less than a year (89% of cases), and type B warts for more than a year (71% of cases). Type I cases rarely bore more than five warts (6% of cases), but type B cases often did so (44% of cases). Type I warts responded better to treatment by curettage and cautery (73% clear) than did type B (36% clear) after a follow-up that varied from eight months to two years. The source of infection was presumed oftener in type I (50% of cases) than in type B warts (18% of cases).

Relationship between Type I and Type B Warts

No case was found in which both types of wart were present simultaneously, and this, together with the clinical distinction which we were able to make between the types, convinced us that the histological change which we have called type I was not a freak finding.

We were unable to define the relationship between the two types of wart. Some facts suggested that type B and type I warts were stages of the same process, and others that the types were entirely distinct entities.

Evidence in favour of the unity of the types was that two of the type I cases which recurred produced type B warts; that three of the series had warts of an intermediate type (Fig. 11) in the sense that foci of intracytoplasmic inclusion bodies occurred in what was otherwise a type B wart; that there were some anomalous cases in which there was a conflict between the clinical and histological appearances, though these cases were few and might be explained by an exchange of labels in the section-cutting department; and that, so far as the series allowed us to judge, the types were equally distributed among the Cambridge schools.

In favour of regarding type B and type I warts as distinct entities was a transmission experiment in which 11 volunteers were scarified with a living wart tissue extract. Six received type I and five type B extract, and all had a control scarification with an extract of normal skin. The controls were negative in every case. Of the five who received the type B extract, three produced warts which were clinically type B; the incubation period was 10 to 12 months. All three warts were puny, and for this reason only one could be verified histologically. Of the six who received the type I extract only one grew a wart. The incubation period was 5½ months, and the wart (Fig. A) waxed fat; after two weeks' growth it was 1.2 cm. in diameter, and alarmed its possessor so much that we were constrained to remove it at once. This wart was type I histologically.

FIG. A.—Experimental wart, about half actual size.

A parallel clinical observation concerned an elderly woman who developed a type I wart on her index finger: the probable source of this wart was her daughter's verruca, also type I. The mother perhaps contracted the wart by darning and washing her daughter's stockings.

Attempts to distinguish by means of skin tests the type of wart from which a given patient was suffering were unsuccessful. The test extracts were formolized, as was the control extract of normal skin, and each patient was tested against type B and type I warts and the control. The type I extract gave reactions in many cases which bore type B warts, in which the type B extract often produced no reaction.

We had hoped that tryptic digestion might free the inclusion bodies from the epidermal cells, as it does in fowlpox (Woodruff and Goodpasture, 1929), but, although we found spherical refractile bodies 3–10 μ in diameter in the digest, they were produced from both types of wart. Dark-ground and electron microscopy failed to demonstrate free elementary bodies in the digest.

Discussion

We have no doubt that type I warts are a clinical and histological entity. Their clinical features are those of the myrmecia of Celsus—a name which means "ant-hill" and describes their domed shape—of the vascular excrescences of Durlacher (1845), and of the plantar warts of Dubreuilh (1895). Celsus (*c.* A.D. 25) said that the roots of these warts were deeply fixed, that they were broad underneath, and that they left a deep cavity after removal. Durlacher commented on the pain and throbbing which they occasioned, and the inflammation and swelling which surrounded them. Dubreuilh described the consistency of the wart substance when felt by the curette as "like wet tow." He mentioned the horny collar which surrounds the warts, and stated that the horn might extend right over the wart and form a roof. Dubreuilh and Celsus recognized that such warts could occur on the palms as well as the soles; we have found that type I warts are commonest on these sites, but also occur beside and under the nails, on the pulp of the digits, and in one case on the face and scalp. Type I plantar warts have room to expand in the thick epidermis of the soles, and in addition are trodden down, hence they are flush with the surface: but on other sites their bulk raises the surrounding skin into the typical dome-shaped lesions which are the origin of the name "myrmecia."

Not all plantar warts were type I, and among those which were not we found that rarer group which are named "mosaic warts" (Montgomery and Montgomery, 1937). This kind is characterized by aggregations of minute warts with polygonal outlines, roughened surfaces, and superficial growth, which are painless and notably resistant to treatment—all features of type B warts.

From the histological side various observers have interpreted the inclusion bodies as a "keratohyalinoid" degeneration. Dubreuilh (1895) described the intracytoplasmic bodies, and Bowen (1907) the intranuclear ones in addition. The first illustration appeared in Martinotti's (1923) paper and showed both intracytoplasmic and intranuclear bodies, though only the former were described in the text. Percival *et al.* (1947) illustrated the bodies, but regarded them as a degeneration preceding involution of the warts. Meirowsky *et al.* (1948) discussed the bodies as inclusions, but their account was

confused by the introduction of the process of "Hornmarkbildung" into the argument. We believe that the process of "Hornmarkbildung" is quite distinct from the inclusion bodies of type I warts, and occurs in both type I and type B warts. The process is concerned with cornification at the tips of the warts' papillae, and is therefore most in evidence in the filiform and digitate warts of the face—the fibrokeratomata of Unna (1880). The essential difference between "Hornmarkbildung" and type I warts is that in the former the nucleus is displaced to one side of the cell, and in the latter remains central. Whatever may be the significance of "Hornmarkbildung," the process is quite distinct from the type I change.

The bodies in type I warts certainly show staining similarities to keratohyalin; but we believe that they are inclusion bodies because they appear constantly in the deepest prickle cells as well as in an occasional basal cell; because not all the epidermal cells are affected; because in the affected cells we can trace a progressive change through the layers of the epidermis; and because the bodies give the staining reactions which would be expected of inclusions, and do not give those which would not be expected. We have been impressed with the resemblance of the histology of type I warts to that of molluscum contagiosum, a resemblance which fails only in that no wart bodies are eventually expelled from the surface of the wart as are the molluscum bodies. The staining reactions of the wart inclusion bodies and of the keratohyalin produced by the unaffected epidermal cells are not identical, for the inclusion bodies are more eosinophilic, and this difference is not explicable simply because of the larger size of the inclusions.

Inclusion bodies in warts have been described by Lipschütz (1924). They were said to be intranuclear and basophilic, and we believe that they correspond with the inclusion bodies which we have described—for example, Fig. 8; we have emphasized the changes in the subgranular layers of the epidermis, and Lipschütz those in the supragranular layers. He did mention the "keratohyalinoid" change, however, and considered that it bore no relation to the inclusion bodies which he was describing. But we have found that the Lipschütz inclusion bodies are confined to the type I warts.

The intermediate type of warts is uncommon. We have found them in association with type B, but never with type I warts. Dubreuilh described one patient whose warts showed a complete transition from the banal to the inclusion type of histology. We have not found a single patient who has borne type B and type I warts simultaneously.

Finally, we would prefer to drop the names type B and type I warts; this nomenclature was convenient at the time, but was intended only to be a makeshift. In the light of the clinical findings we consider that the type B wart should remain as "verruca vulgaris," while the type I wart should be dignified with its old name, "myrmecia."

Summary and Conclusions

We have found inclusion bodies in some warts: such we have called type I (inclusion) warts, in order to distinguish them from type B (banal) warts, which have a commonplace histology devoid of inclusions.

The inclusion bodies are eosinophilic and are both intracytoplasmic and intranuclear; they appear first in the lowest layer of prickle cells, and their development can be followed into the stratum corneum. The bodies stain as inclusion bodies would be expected to do.

The distinction between type B and type I warts is clinical as well as histological. Type I warts are usually plantar, palmar, subungual, or paronychial; they are painful and often associated with "inflammation" of the surrounding skin; they are deeply set in the skin and form dome-shaped swellings; when curetted their size is greater than appears on the surface, and their substance is opaque, white, and soft.

We are uncertain of the relationship existing between the two types, but some evidence—the recurrence of some type I warts as type B, and the discovery of an intermediate type—suggest that type I warts are a variety of type B. However, other evidence—a transmission experiment and a clinical case in which the warts bred true—points towards an absolute distinction between the types.

The type I wart is the same entity as the myrmecia of Celsus, the vascular excrescence of Durlacher, and the plantar wart of Dubreuilh. Those plantar warts called the mosaic type are histologically type B.

The type I change is quite distinct from the process known as "Hornmarkbildung."

The basophilic intranuclear inclusion bodies of Lipschütz are the supragranular stage of the inclusion bodies of type I warts.

We suggest that the name "verruca vulgaris" be confined to type B warts, and that type I be renamed "myrmecia."

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ADDENDUM.—Since submitting this paper we have seen two reports by Strauss *et al.* (1949, 1950). These authors centrifuged ground wart tissue and found small elementary bodies in type I warts, but none in type B. We are now attempting to repeat this observation.

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CLINICAL SYNDROME ASSOCIATED WITH KIMMELSTIEL–WILSON LESION OF THE KIDNEY

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[WITH SPECIAL PLATE]

The liability of the diabetic patient to develop kidney disease is due in part to the more frequent occurrence and severe nature of infections, ranging from pyelitis to necrotizing renal papillitis, and in part to degenerative disease of the renal arteries and arterioles. The clinical criteria for recognizing these complications have been established. But diabetics are also subject to a renal disease called "intercapillary glomerulosclerosis" by Kimmelstiel and Wilson (1936), which is probably peculiar to diabetics, and for the recognition of which during life there are as yet no accepted clinical criteria.

Several clinical and pathological studies of intercapillary glomerulosclerosis have appeared since the original observations, many tending to confirm that the typical lesions are associated with a recognizable syndrome, but others describing cases in which no syndrome was discerned. More recently, Kimmelstiel and Porter (1948) have done much to clarify this position by suggesting that two distinct and possibly different lesions have been recognized in the literature as intercapillary glomerulosclerosis—a diffuse form in which there was only a widespread basement membrane thickening and a nodular form in which there are distinct well-defined islands of hyaline material in the glomeruli. They observe that the evidence of the literature shows that the "nodular" type is a lesion found only in diabetics, and that these diabetics had usually shown a definite syndrome. Further, as the original paper of Kimmelstiel and Wilson refers clearly to cases showing the "nodular" form, only such a lesion should be described as "intercapillary glomerulosclerosis" or the Kimmelstiel–Wilson lesion. This procedure has been adopted in this paper.

A comparison between the clinical syndrome recorded in association with different types of renal disease in diabetics should show whether there was a syndrome associated with the lesion, at least in its advanced stages. We decided to make such a comparison after analysing the clinical records and post-mortem material of all diabetics coming to necropsy in Hammersmith Hospital from July, 1936, to August, 1948. The cases were classified according to their renal condition into one of the five groups shown below, and a comparison made between the clinical features of these five groups provides the results presented.

Pathological Grouping

There were 46 cases. Three were discarded, as adequate pathological material was not available. There were no cases of nephritis. The remaining 43 were placed in the following groups:

Group 1: the Kimmelstiel–Wilson Group (11 cases; 8 with lesions in nearly every glomerulus, 3 in only occasional glomeruli).—All cases showing nodular intercapillary glomerulosclerosis as described by Kimmelstiel and Wilson were placed in this group, irrespective of other disease conditions—that is, all cases showed the following features: (*a*) Discrete hyaline islands in the glomeruli (Plate, Fig. 1). The capillaries around them appeared to remain patent and even, in places, dilated (Fig. 2). (*b*) A pronounced degree of arteriosclerosis (Fig. 1). This may be seen to affect both afferent and efferent arterioles (Fig. 3). (*c*) A hyaline "cap" on a thickened Bowman's membrane (Fig. 1). In some cases special stains were employed which showed the protein nature of the hyaline material (Fig. 3), the fatty changes in it and in the adjacent tubules (Fig. 4), and the argentophil staining of the hyaline balls (Fig. 5).

Group 2: the Arteriolosclerotic Group (three cases).—This consisted of those cases in which arteriolosclerosis was present without the typical Kimmelstiel–Wilson lesions (Fig. 6).

Group 3: the Arteriosclerotic Group (4 cases).—This was composed of those cases which showed arteriosclerosis, both macroscopically and microscopically, but no Kimmelstiel–Wilson lesions.

Group 4: the Pyelonephritic Group (four cases).—This consisted of those cases in which pyelonephritis was the dominant lesion and no Kimmelstiel–Wilson lesions were noted.

Group 5: the "Other Diabetic" Group (21 cases).—This group included all the remaining cases which showed no more permanent renal change than "cloudy swelling," "fatty degeneration," or "toxic change."

Results

Comparison of the recorded clinical features of these five groups with different renal pathological conditions showed that the groups also differed in their clinical features. The tables show the number of records giving adequate information on each point examined. Though the groups were small, several of the differences appeared significant, and attention is drawn below to those which seem to help to delineate the syndrome associated with Kimmelstiel–Wilson lesions.

Age and Sex.—The distribution (Table I) confirmed the usual finding that intercapillary glomerulosclerosis involves the elderly female especially.

TABLE I.—*Age and Sex Incidence*

	Renal Pathology Group				
	1 (11 Cases)	2 (3 Cases)	3 (4 Cases)	4 (4 Cases)	5 (21 Cases)
Mean age at death	69·1	52	69	48·2	51·2
Range of ages ..	52–81	41–73	60–75	18–80	12–81
No. of females ..	10	3	2	1	11

Diabetes.—An attempt was made to classify the diabetes according to its severity and controllability so far as the available records permitted. Cases which had been satisfactorily controlled for long periods without insulin were classed as mild; those which always required more than 20 units of insulin daily were classed as severe. Patients whose symptoms disappeared and who gained and maintained weight without incident were assessed as "easily controlled"; and those whose symptoms recurred or who needed more than an initial hospital admission for stabilization or coma were assessed as difficult to control. No clear difference could be distinguished between these small pathological groups in these respects. In view of previous observations it is worth noting that the Kimmelstiel–Wilson group showed instances of both severe and mild cases, some easily controlled and

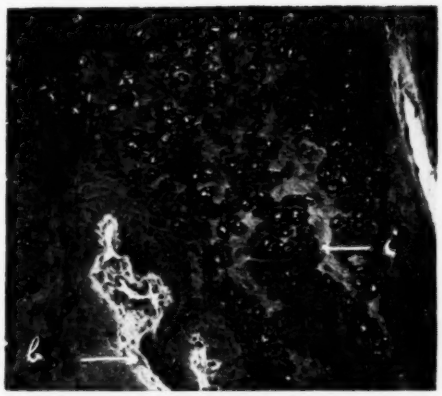

FIG. 1

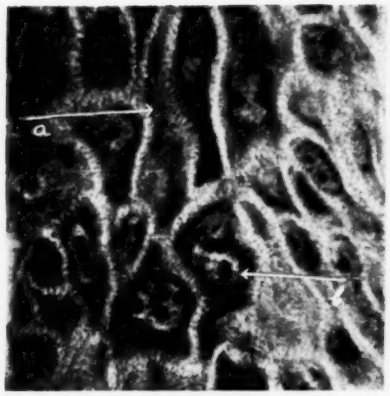

FIG. 2

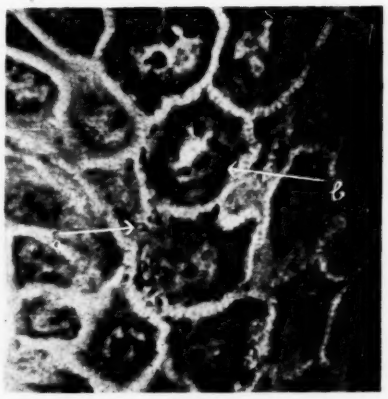

FIG. 3

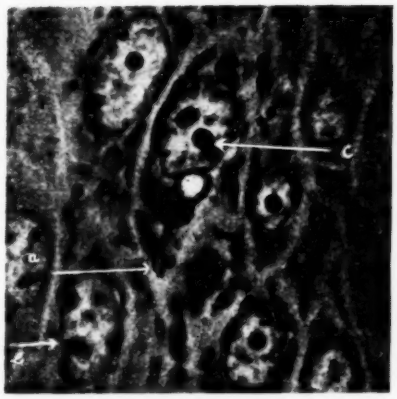

FIG. 4

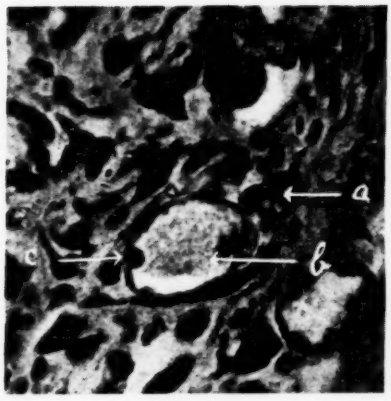

FIG. 5

FIG. 6

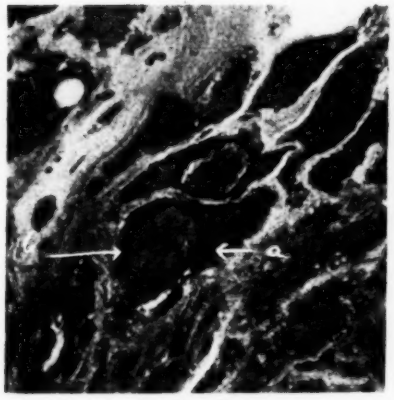

FIG. 7

FIG. 8

FIG. 9

FIG. 10

FIG. 1.—Wart, type I. (× 90.) b = Basal-cell layer. i = Inclusion bodies.

FIGS. 2–10.—Wart, type I. (× 900.) Development of inclusion bodies in successive epidermal layers. a = Intracytoplasmic inclusions. b = Nuclei of affected cells. c = Intranuclear inclusions (Cowdry, type B). Eosinophilic structures appear dark in the photographs. Sections at the level of the lower prickle cells (Fig. 2), middle prickle cells (Figs. 3 and 4), upper prickle cells (Fig. 5), granular layer (Fig. 6), and horny layer (Figs. 7–10).

FIG. 11.—Wart, intermediate type. (× 90.) i = Inclusion bodies, in clumps.

FIG. 11

I. GILLILAND: KIMMELSTIEL-WILSON LESION

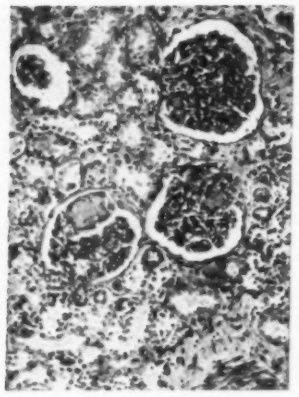

FIG. 1. — Kimmelstiel-Wilson lesion, Group 1. General picture. (H. & E. × 60.)

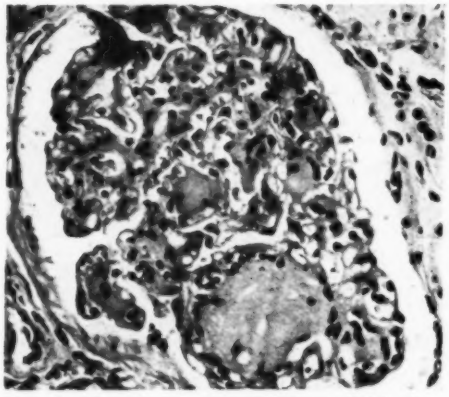

FIG. 2.—One large and several small islands. (H. & E. × 173.)

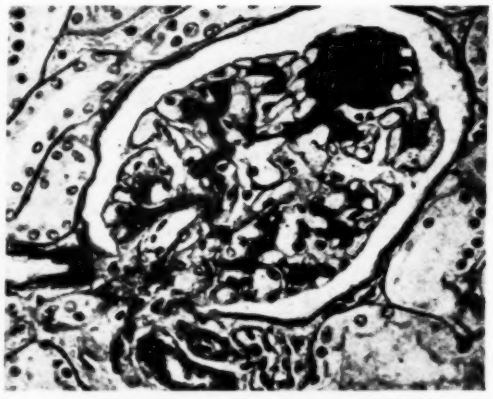

FIG. 3.—Both afferent and efferent arterioles are affected. (Periodic acid of Schiff. × 205.)

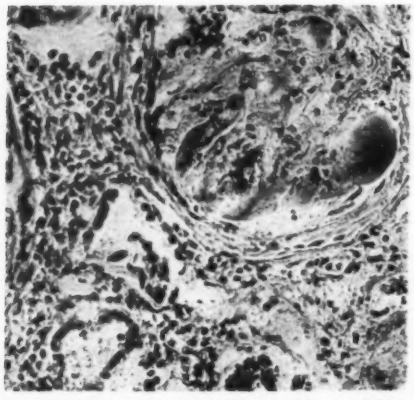

FIG. 4.—Fatty changes. (Sudan IV. × 205.)

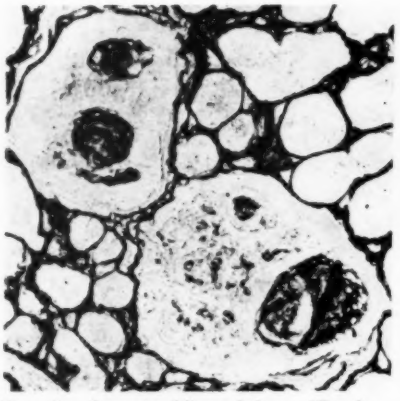

FIG. 5.—Argentophil nodules. (Gordon and Sweet's modification of Wilder. × 205.)

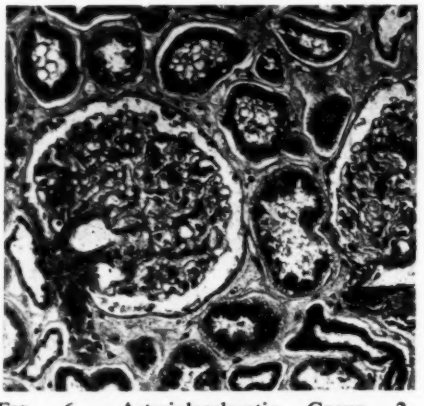

FIG. 6. — Arteriolosclerotic Group 2. Arteriolosclerotic kidney. (H. & E. × 205.)

J. Ll. TEMPLE: BENIGN CALCIFIED EPITHELIOMA

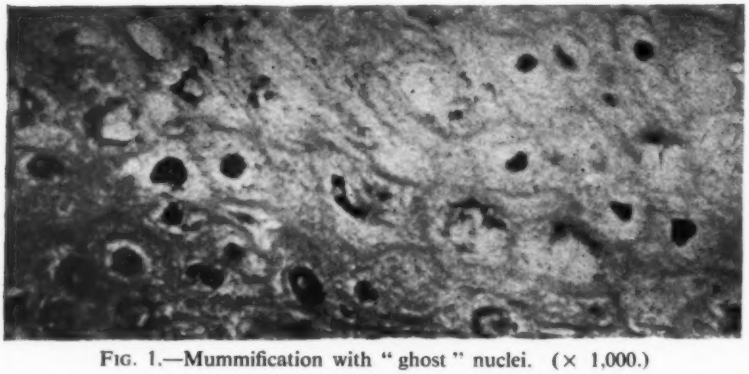

FIG. 1.—Mummification with "ghost" nuclei. (× 1,000.)

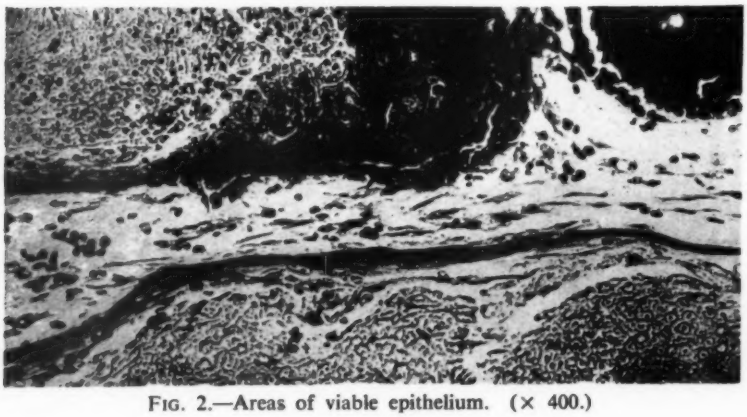

FIG. 2.—Areas of viable epithelium. (× 400.)

FIG. 3.—Bone formation. (× 400.)

others not. There were no severe diabetics in the arteriosclerotic group, and all the pyelonephritic group were difficult to control.

Urinary Finding and Renal Function (Table II).—Proteinuria characterized all groups of permanent renal disease, and was found in the "other diabetic" group

TABLE II.—*Renal Tests*

	Renal Pathology Group				
	1 (10 Cases)	2 (3 Cases)	3 (3 Cases)	4 (4 Cases)	5 (21 Cases)
Proteinuria +++	7	2	—	3	1
,, + ..	10	3	3	4	6
Urinary-tract infection	6	2	2	4	4

only in tests made during the course of a terminal coma. A heavy and persistent proteinuria seemed to characterize the Kimmelstiel–Wilson group and the pyelonephritic group. Urinary infection was judged to be present when a catheter specimen of urine had shown pus cells and given a positive culture, or when clear post-mortem evidence of renal pelvic inflammation was found. Infection was a frequent feature of all groups with permanent renal trouble. There were insufficient observations to compare the incidence of renal failure and anaemia.

Hypertension and Heart Failure (Table III).—The one Kimmelstiel–Wilson case which was not recorded to have hypertension, on the standard of 150/90 as the

TABLE III.—*Hypertension and Heart Failure*

	Renal Pathology Groups				
	1 (10 Cases)	2 (3 Cases)	3 (3 Cases)	4 (4 Cases)	5 (21 Cases)
Mean B/P ..	182/96	144/82	187/102	132/77	148/76
No. recorded to be in failure ..	8	1	1	—	1
No. with raised J.V.P.	6	1	—	—	1
No. with paroxysmal nocturnal dyspnoea	3	1	—	—	—

upper limit of systolic and diastolic pressure respectively, was admitted in heart failure from which she did not recover. At necropsy her heart weighed 410 g. and had two myocardial infarcts, so it seems reasonable to assume that she had previously been hypertensive.

Oedema.—All the cases of the Kimmelstiel–Wilson group had oedema, at least of the dependent parts, while in four cases it extended beyond the legs and sacrum, which was not shown in the other groups. Two arteriolosclerotics revealed oedema of the ankles, as did three of the "other diabetic" group.

Peripheral Neuropathy.—Symptoms suggesting peripheral neuropathy are often found in the diabetic without easily demonstrable physical signs. Records noting complaints of darting or lancing pains, or paraesthesiae, such as burning, numbness, or tingling in the limbs, were classed as relevant subjective symptoms. Where note was made of muscle tenderness, sensory loss, or absent tendon jerks, these were classed as objective signs. Such peripheral neuropathy was recorded as more frequent and more obvious among diabetics found to have Kimmelstiel–Wilson lesions than among other groups. Ankle tendon jerks were absent in all but one of the Kimmelstiel–Wilson group, the remaining one showing subjective symptoms.

Eye Changes.—Eye changes were a feature of all Kimmelstiel–Wilson cases, retinopathy being present in all cases in which the fundus was not obscured by cataract. In three cases it was severe enough to make the patient "virtually blind," in contrast to the infrequent and relatively symptomless eye changes in the other groups.

Summary of Results (Table IV)

Thus, while proteinuria and urinary-tract infection were features of all the groups with renal disease, other clinical features were almost universally present in the cases with Kimmelstiel–Wilson lesions, and not found together in any other group.

TABLE IV.—*Clinical Features of the Kimmelstiel–Wilson Syndrome Among Renal Pathology Groups*

	Renal Pathology Groups				
	1 (10 Cases)	2 (3 Cases)	3 (3 Cases)	4 (4 Cases)	5 (21 Cases)
Suggestive:					
Proteinuria ..	10	3	3	4	6
Urinary infection	6	2	2	4	4
Hypertension—over 150/90 ..	9	1	3	1	4
Probable:					
Heart failure ..	8	1	1	—	1
Oedema of ankles or more ..	10	2	—	—	3
Retinopathy or obscured by cataract ..	10	1	—	1	6
Peripheral neuropathy	9	2	2	—	5
No. showing all the above probable symptoms ..	8	—	—	—	—

These non-renal clinical features which seem to distinguish diabetes with Kimmelstiel–Wilson lesions from diabetes with other pathological conditions of the kidney were: Hypertension with heart failure; peripheral neuropathy; oedema at least of the dependent parts; and retinopathy or obscuring cataracts. These features were rare in the other groups studied, and in none were all four features present in the same patient.

Discussion

Attention has recently been drawn to the fact that the kidneys of the diabetic are peculiarly liable to disease of more than one sort. Of the 43 fatal diabetic cases reviewed in this paper 51% had irreversible kidney conditions, 25% showing intercapillary glomerulosclerosis, often in addition to evidence of arterial disease, while 44% of all cases showed evidence of urinary infection. Millard and Root (1948) found that 52% of 110 diabetics examined post mortem showed well-marked kidney disease, and in 23.5% there were two or more forms of kidney disease present. Bell (1946) showed arteriosclerosis to be five times as frequent in the diabetic over 50 as in a control group of a similar age, while Baldwin and Root (1940) found renal infection five times more often in diabetics compared with others examined post mortem. Indeed, urinary infection has been found to be an important cause of death in the diabetic (Robbins and Tucker, 1944). The incidence of the Kimmelstiel–Wilson lesion was found to be 17% in the summary of the literature by Kimmelstiel and Porter.

Many authorities (Bell, 1946; Kimmelstiel and Porter, 1948) agree that the lesions are almost pathognomonic of diabetes. Some authors, considering diffuse glomerular hyalinization without island formation

as a lower grade of the lesion, have found it also in non-diabetics (Horn and Smetana, 1942), but concede that the "advanced" form is always associated with diabetes. Kimmelstiel and Porter acknowledge that a few cases with typical "nodular" lesions were not known to be diabetic. Some of these may have had such mild diabetes as to escape notice. Rifkin *et al.* (1948) refer to two such cases. However, Bell (1946) has seen only one exception—a patient with primary hypertension who was studied for several months before death and at no time showed either hyperglycaemia or glycosuria. Bell also believes that the hyaline masses of chronic glomerulonephritis are easily distinguishable from the nodular diabetic lesions.

Recent studies have tended also to confirm Kimmelstiel and Wilson's observation that a recognizable clinical syndrome is associated with these lesions, of which "the constant features are diabetes, albuminuria, hypertension, and retinal vascular disease" (Newburger and Peters, 1939). Kimmelstiel and Porter find that "in a patient 50 or more years of age with chronic diabetes, nephrotic oedema, and albumin in the urine with a high blood cholesterol one can safely make the diagnosis of intercapillary glomerulosclerosis with 100% accuracy," adding that "advanced retinopathy, specifically of the diabetic type, is more or less regularly associated with intercapillary glomerulosclerosis."

One method of study, however, has shown that proteinuria, urinary infection, and indices of impaired renal function are not of exclusive diagnostic value. Infection, for instance, which is frequent and often asymptomatic in the diabetic (Harrison and Bailey, 1942) is a likely complication of any diabetic renal disease and not a finding which can exclude other conditions as Gauld *et al.* (1948) would seem to suggest. Even in the most severe infection of renal papillitis 12 of the 26 described by Edmondson *et al.* (1947) show Kimmelstiel–Wilson lesions. Uraemia supervened only in one of our cases and in 17.7% of the series reviewed by Kimmelstiel and Porter. We are examining the suggestion of Rifkin *et al.* (1948) that doubly refractile bodies in the urine are of diagnostic importance.

Two other renal conditions not present in our series may closely simulate intercapillary glomerulosclerosis—chronic nephritis and amyloidosis. The nephrotic stage of chronic glomerulonephritis is more likely to occur in the younger age group, and may give a characteristic history of previous acute onset (Newburger and Peters, 1939; Henderson *et al.*, 1947). Kimmelstiel and Porter show that repeated Addis counts should enable the diagnosis of glomerulonephritis to be made, as haematuria of significant degree is not found in intercapillary glomerulosclerosis. Amyloid disease is rare in diabetes (Newburger and Peters), and the characteristic anaemia and symptoms referable to the primary disease would serve to differentiate this condition.

Others have commented upon the four clinical features which we believe to form a recognizable syndrome.

Hypertension with heart failure was noted to be present in the brief clinical notes accompanying the original pathological studies of Kimmelstiel and Wilson and to be common among the cases of Siegal (1940) and Siegal and Allen (1941). Rifkin *et al.*, in a series of 22 necropsies on patients with intercapillary glomerulosclerosis, found that 95% had had systolic hypertension and 90% had had diastolic hypertension, and 93% were observed to have been in heart failure. Two of those who did not show hypertension had histories and electrocardiographic evidence of recent myocardial infarction. On the other hand, Mann *et al.* (1949), choosing their cases deliberately from younger patients, found that although hypertension was a universal sign it did not become severe until late in the disease—a view held also by Kimmelstiel and Porter.

Widespread oedema was present in four of the original cases described by Kimmelstiel and Wilson, and a "nephrotic syndrome" with oedema and lowered serum proteins has often been described as part of the syndrome (Derow *et al.*, 1939). A "nephrotic syndrome" was present in 1 out of 10 cases described by Herbut (1941) and 3 out of 10 described by Siegal and Allen (1941). Laipply *et al.* (1944) found a nephrotic syndrome in only 6.5% of cases. Kimmelstiel and Porter, summarizing the literature, state that oedema of a nephrotic type is present in less than 10%. Mann *et al.* have suggested that hypoproteinaemia is a relatively late and generally a terminal finding, but that oedema alone was an early sign, and in females often the first. Our series, as those of Rifkin *et al.*, would suggest that the presence of oedema, even if limited to the dependent parts, is significant in conjunction with the other evidence.

Siegal (1940) and Siegal and Allen (1941) first described peripheral neuropathy as part of the syndrome. Others, such as Rifkin *et al.*, have noted simply that peripheral neuropathy was a complication, but do not give details of their records. Rundles (1945) thinks that the coincidental finding of retinopathy and neuropathy is more than fortuitous. In our series we found that subjective symptoms coupled with absent jerks were an almost universal finding.

Newburger and Peters found retinopathy in all their Kimmelstiel–Wilson cases. Kimmelstiel and Porter's analysis of the literature showed retinopathy to have been recorded in 86% of cases. Ashton (1949) has suggested that microscopical examination of the retina would show a higher figure, as he confirms the findings of Ballantyne (1946) that microaneurysms can be found in the retinae of diabetics who did not appear to have clinical retinopathy in life. The severity of the retinopathy is remarked upon by Henderson *et al.* (1947), while Von Bahr (1947) thought that the most severe proliferating type of retinopathy was almost always associated with the Kimmelstiel–Wilson lesions of the kidney. Friedenwald (1948) suggested, and Ashton (1949) agreed, that the intercapillary glomerulosclerosis and diabetic retinopathy are manifestations of the same vascular process.

It is generally agreed that most cases of intercapillary glomerulosclerosis occur between the ages of 50 and 70, and that females are affected twice as often as males (Kimmelstiel and Porter), yet these features are not of diagnostic importance. Cases have been recorded in younger age ranges (Laipply *et al.*, 1944; Goodof, 1945; Mann *et al.*, 1949) and in severe diabetes (Herbut, Mann *et al.*). The question of control is more difficult to assess, depending as it does on long-term continued observations. It is unlikely that any diabetic control is perfect, and satisfactory evidence is not obtainable except of the frequency of the grosser manifestations of bad control. There has always been a clinical impression that badly controlled diabetics were more

likely to suffer from complications such as neuropathy (Rundles) and retinitis proliferans (Waite and Beetham, 1935). Yet others have claimed that the treatment of diabetics had no bearing on the renal involvement (Kimmelstiel and Porter, Laipply *et al.*, Henderson *et al.*).

The duration of the diabetes, though also difficult to assess, seems to be important, and the view has been put forward (Dolger, 1946) that the duration was the most important factor in the development of degenerative lesions. Henderson *et al.* showed that in their series the duration of the diabetes appeared to be short only where the nature of the diabetes was mild, and may well have been present without symptoms for some time. Their series showed that when advanced lesions were present the duration of diabetes averaged 11.2 years, where mild lesions were present 8.1 years, and where no lesions were present 5.2 years. Goodof showed a steady rise in the incidence of intercapillary glomerulosclerosis among diabetics arranged in order of duration after six years had passed. Mann *et al.* also found a significant relation of the lesion with duration of diabetes, the average duration of their younger group of diabetics being 14.8 years.

On the other hand, Croom and Scott (1949) could find no correlation between the severity and control of diabetes and the onset of complications, and showed clearly that degenerative lesions were not inevitable. Their study of 60 diabetics selected to have an average duration of over 15 years showed 15 free from any clinically recognizable degenerative disease, one of whom had been diabetic for 26 years. In their group there were only two with albuminuria and oedema. Thus if degenerative complications are not inevitable with prolonged diabetes, and, less certainly, if control makes little difference, some other factor may be involved. These complications may be due either to prolonged diabetes in some special circumstances with which we are not as yet familiar or to prolonged diabetes of a special type, or to both.

Our study, coupled with an analysis of the literature, leads us to conclude that a syndrome including diabetes, albuminuria, and all the following four features—hypertension with heart failure, diabetic retinopathy or obscuring cataract, peripheral neuropathy, and oedema at least of the dependent parts—will reasonably imply the presence of intercapillary glomerulosclerosis in the kidney.

Summary

Among 43 diabetics examined post mortem the following groups of renal conditions were found: 11 with Kimmelstiel–Wilson lesions (with or without other lesions); three with arteriolosclerosis (without other lesions); four with arteriosclerosis (without other lesions); and four with pyelonephritis (without other lesions). The remaining 21 cases were classed as "other diabetics," without irreversible renal conditions.

Analysis of the associated clinical picture showed that: (*a*) The Kimmelstiel–Wilson group comprised, especially, elderly females who had had a mild diabetes for many years. (*b*) All groups with renal disease were associated with proteinuria and, more frequently than other diabetics, with urinary infection. (*c*) The Kimmelstiel–Wilson group, however, almost universally, showed in addition all the following features: hypertension with heart failure; peripheral neuropathy; oedema at least of the dependent parts; and retinitis or cataract obscuring the retina. This syndrome was not found in any other group.

It is suggested that in any diabetics who show proteinuria the presence of the four additional features listed above implies Kimmelstiel–Wilson lesions in the kidney.

My thanks are due particularly to Dr. Russell Fraser for help in preparing the clinical material; to Dr. I. Doniach and Dr. R. Pearce for help with the pathological material; and to Mr. Willmot of the photographic department.

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The First International Congress on Diseases of the Chest, sponsored by the Council on International Affairs, American College of Chest Physicians, held at the Carlo Forlanini Institute, Rome, Italy, September 17 to 22, was attended by approximately 1,000 physicians and their wives. At the inaugural session the College medal was presented to Sir Alexander Fleming for his discovery of penicillin. More than 100 scientific papers were presented during the congress by physicians from 40 countries, including two delegates from the Soviet Union, Professor Pavel Lukomski, who read a paper on "Aetiopathogenesis of Suppurative Diseases of the Lung," and Professor Feodor Uglov, who read one on "Lung Resection Ligation of the Pulmonary Artery in the Treatment of Chronic Suppurative Lung Diseases." Special administrative meetings of the governors and regents of the College from the 40 countries represented at the congress were held. A European Chapter of the College was organized, with Dr. André Meyer, Paris, as the general secretary. The regents of the College in Europe who will serve as the executive council for the Chapter are Professor Gustav Maurer, Davos, Switzerland; Professor Etienne Bernard, Paris, France; Professor Lopo de Carvalho, Lisbon, Portugal; Professor Nicholas Oekonomopoulos, Athens, Greece; Professor Eugenio Morelli, Rome, Italy; and Sir Alexander Fleming, London, England. Delegates from England who attended the congress in Rome were Sir Alexander Fleming, Sir Harold Boldero, and Drs. A. J. Benatt, C. K. Cullen, M. L. Dowldar, W. Griffel, W. Paton Philip, R. R. Trail, M. Weinberger. The delegates were received by his Holiness, Pope Pius XII, and a reception was held for the visiting delegates by Signor Salvatore Rebecchini, Mayor of Rome.

BENIGN CALCIFIED EPITHELIOMA

BY

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[WITH SPECIAL PLATE]

Since Malherbe (1880) first gave an account of a circumscribed calcified lesion of the skin and named it "épithélioma calcifié" a number of papers have been published on this interesting condition. The more useful in the English language are Ch'in's (1933) comprehensive review of the world literature, and papers by Côté (1936), Highman and Ogden (1944), and King (1947), all in journals of pathology. The standard textbooks of general pathology make no reference to the condition, Willis (1948) alone giving a brief description and discussing its aetiology. Of the standard textbooks of surgery consulted only Aird (1949) mentions it, quoting Willis.

For this reason the lesion is rarely, if ever, recognized clinically, and yet it is not uncommon, as the following eleven cases show, ten occurring in 11,330 surgical specimens examined during 1943 to 1949 in the histological laboratory of a general hospital, and one found from the records of another hospital.

Clinical Findings

Analysis of the case records of the present series (see Table) reveals several characteristic features. The lesion

Table Showing Details of Cases

Case No.	Sex	Age	Site	Injury	Clinical Diagnosis	Viable Epith.	Calcification	Bone	Giant Cells	Pigment
1	F	7	Arm	+	Implantation dermoid fat necrosis	–	+	+	+	–
2	M	49	Leg	–	Fibroma	–	+	–	–	+
3	F	29	Neck	–	Calcified sebaceous cyst	–	+	+	+	–
4	F	14	Face	–	Calcified gland	+	+	–	+	+
5	F	60	,,	–	Sebaceous cyst	+	–	–	+	–
6	F	?	Arm	–	,, ,,	–	–	–	–	–
7	M	65	,,	–	Secondary carcinoma	–	+	+	–	–
8	M	19	,,	+	Cyst	–	+	+	+	–
9	F	11	Face	–	,,	–	+	–	–	–
10	F	2½	,,	+	Foreign body	–	+	–	+	–
11	F	63	Chest	–	Sebaceous cyst	+	+	–	+	–

may occur at all ages, the youngest in this series being 2½ years and the oldest 65, but half the cases were subjects under 20. This low age incidence has been noted previously, and may be of importance in considering the aetiology.

Females predominated over males in the proportion of 8 to 3, and four cases were girls under 14 years of age. In Côté's series, however, males were more common, and in those of Ch'in and of Highman and Ogden the sexes were equal. There does not appear to be any significance in the sex distribution, though Côté suggests that females may seek advice more often for cosmetic reasons.

Length of history varies from months to years and increase in size is slow. In three cases there was a history of injury some years previously. Pain was rarely complained of, and the tumour was removed for reasons of appearance or because of its uncertain nature.

The physical characters were constant. The lesion was a well-defined nodule in the subcutaneous tissue, varying from 5 to 25 mm. in diameter. It was usually described as hard or firm and when excised was finely nodular with a gritty cut surface (Fig. A). Attachment to the skin was commonly noted but never to the deeper structures.

The usual distribution was confirmed, the nodule occurring in five cases about the head and neck, four times on the arms, once on the leg, and once on the chest.

Diagnosis and Treatment

If these characteristics are borne in mind a confident diagnosis of benign calcified epithelioma should be possible, but it is not made because the condition is not sufficiently well known. Reading through the case records it can be seen that the clinicians were impressed by the two factors of hardness and attachment to skin. On these grounds the most frequently made diagnosis was calcified sebaceous cyst, usually preceded by several queries. Yet it is of interest that during the seven years under review only one specimen of this condition was submitted to microscopy.

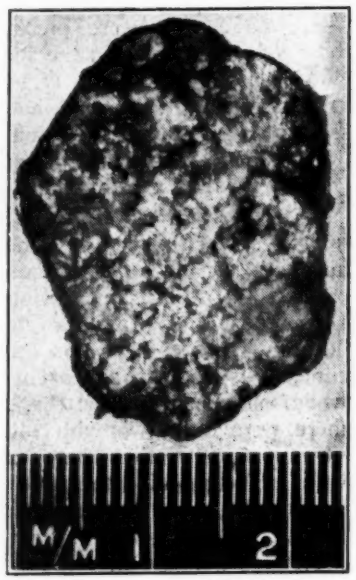

FIG. A.—Cut surface of the tumour, showing patchy calcification.

In one case the lump was thought to be a secondary deposit from carcinoma of the bronchus and was removed for biopsy. Other diagnoses, usually tentative, were sequestration dermoid, foreign body, subcutaneous fat necrosis, and the ubiquitous fibroma.

Treatment is by surgical excision, usually under local analgesia, but a general anaesthetic will be necessary for a child. Recurrences have been reported, but these probably follow incomplete removal due to ignorance of the nature of the condition at the time of operation.

Histology

The cases here reported all showed in some degree the characteristic histological features previously described by other authors. Decalcification was usually necessary in the preparation of the material. Microscopical examination of the lesion showed in each case masses of epithelial cells surrounded by a well-defined fibrous capsule. The cells had undergone necrosis, their nuclei failing to stain, but still retained their faint cell outlines with "ghost" nuclei, a change sometimes termed mummification and the most typical feature of the condition (Plate, Fig. 1). There may be areas of viable epithelium, smaller in extent and sometimes absent altogether, which retain their normal staining reactions (Fig. 2).

Patchy calcification of the mummified epithelium is nearly always present in varying amount, but is not

essential to the diagnosis and was absent in Cases 2, 5, and 6. Ossification also occurs (Fig. 3), and was present in four cases in this series (Cases 1, 3, 7, and 8). A well-marked fibrous stroma is present in which foreign-body giant cells are a frequent occurrence. Melanin-like pigment was noted in Case 4 and has been recorded in previous series. In Case 2 eleidin granule pigment was demonstrated, and no previous references to this have been found in the literature.

Discussion

The essential feature of the lesion seems to be an encapsulated proliferation of epithelial cells, followed by their death. Calcification and later ossification can be considered as secondary changes apt to occur in any dead tissue. The result is easily recognized under the microscope, but the origin of the condition is obscure and many theories have been propounded.

Côté considers it to be a neoplasm of low malignancy, intermediate in type between a sebaceous cyst and a basal-celled carcinoma, founding his theory on the presence of mitotic figures and a supposed basal origin for the epithelium. This supposition is disputed, for in cases in which viable epithelium was present this appeared to be squamous-celled in origin.* Confirmation was afforded in Case 5 by the presence of prickle cells and keratinization; in Case 2 eleidin granules were present, which normally occur in the stratum granulosum, and are further evidence of the squamous nature of the epithelial cells. No mitotic figures were noted in the present series. Moreover, it is unusual for sebaceous cysts or rodent ulcers to occur in the low age group of benign calcified epithelioma.

Highman and Ogden found brown pigment resembling melanin in three cases out of twelve, and suggested that the primary lesion is an epidermoid cyst arising from a hair follicle, with which pigment is often associated.

Willis regards the condition as being due to degenerative changes in the proliferating epithelium of a sebaceous or epidermoid cyst and does not think the lesion is a true tumour.

King differentiates two types—one derived from squamous cells proliferating in an epidermoid cyst, and the other, much less common, of basal cells with mitotic figures. In support of his first suggested form he found transitional types showing the characteristic changes of mummification occurring in an otherwise typical epidermoid cyst.

Epidermoid cysts may arise from epidermal cells implanted by injury, from sebaceous ducts or from hair follicles. The histological appearances in this series are consistent with an origin from such a cyst and do not support an origin from basal cells or indicate any neoplastic change. A history of trauma in three cases and the usual occurrence of the lesion in situations exposed to minor injury suggest that the cyst may sometimes be of the implantation variety.

Summary

Eleven new cases of benign calcified epithelioma are reported.

The clinical findings and histology are described.

The nature of the lesion is discussed and evidence presented in support of an origin from proliferation of squamous cells in an epidermoid cyst.

A plea is made for the wider recognition of a not uncommon skin condition.

I am indebted to members of the staff of the West Middlesex Hospital for permission to publish their cases, and to Dr. H. Rogers, of Hillingdon Hospital, for details of Case 11. My thanks are due to Dr. A. C. Counsell for much helpful advice with the histology, and to Mr. Vinton for the photographs.

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GLINSKI AND THE AETIOLOGY OF SIMMONDS'S DISEASE (HYPOPITUITARISM)

BY

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In studying the literature for early observations on lesions of the pituitary gland, Simonds (1922) referred to a German abstract of a paper by Glinski (1913b) in which two cases of post-partum necrosis of the pituitary were described; this abstract was later mentioned by Sheehan (1937). I was unsuccessful in tracing in this country the original Polish paper, but further references were kindly supplied me by Dr. J. J. Keevil, librarian keeper of the Royal College of Physicians of London. These papers, however, also could not be traced in this country. An approach was then made to the Director, Army Medical Library, Washington, D.C., and as a result three papers by Glinski, two of which are in Polish, have been traced (1913a, 1913c, 1913d), the microfilms of them seen, and translations made.

Glinski's Investigations

Glinski's papers provide most interesting reading, particularly when it is appreciated that they were written some 37 years ago. He drew attention to work which had been done on such properties of extracts of the posterior lobe of the pituitary as the production of increased arterial blood pressure, peripheral vasoconstriction, slowing of the pulse, contraction of smooth muscle, especially of the uterus and urinary bladder; and the lack of work done on the properties of anterior-lobe extracts. This he ascribed to the difficult procedure of obtaining extracts, and he warned against the danger of drawing conclusions from impure or contaminated extracts.

In other words, the extract of a gland was not necessarily the secretion of the gland. "In my opinion, therefore, we should not, at the present stage of our knowledge, overestimate the effects of the hypophysial extracts, and, in spite of many contradictory findings based on these investigations, I still regard the anterior glandular part of the pituitary as the active and more important division of the gland." He based his views on an extensive study of the anterior lobe, its "incomparably greater blood supply," and the

* This is not true. Côté describes basal-cell epithelium in most of his cases as well as squamous cell epithelium.

histopathological changes present in acromegaly, gigantism, and dystrophia adiposogenitalis. A better approach, he said, would be to study the anterior pituitary in all diseases wherever possible.

He then drew attention to certain specific and significant signs and symptoms associated with anterior pituitary damage, such as irregular menstruation, complete amenorrhoea, changes in the secondary sex characteristics, loss of libido, and atrophy of the sex glands. This led him to extend the observations of Erdheim and Stumme (1909) by a post-mortem study of pituitaries in 28 males and 49 females, the latter including pregnant women, women who died during labour, nursing mothers, and women who had never been pregnant. In virgins the gland weighed 0.58 g., in non-pregnant women 0.70 g., in pregnancy of 5–8 months 0.84 g., in pregnancy up to parturition 0.92 g., to reach a peak of 0.95 g. for women in labour up to four weeks after labour. He maintained that the involution of the gland was slow following childbirth, began to take place two weeks later, and was noticeable macroscopically only in the second month after childbirth, but no full restitution took place even up to the seventh year after pregnancy. The enlargement of the gland, both by weight and by measurement, began in the middle of pregnancy and affected only the anterior lobe. He also found that in women who died during labour from severe acute blood loss the enlargement of the pituitary remained. The colour of the gland in pregnancy was pale, almost white, compared with the reddish-brown colour of the normal pituitary, and this was due to the poor supply of blood to the pituitary in pregnancy.

The cause of the enlargement of the pituitary in pregnancy he believed to be due to changes in ovarian activity, inhibited ovulation, and formation of corpus luteum. As castration in man and animals produced enlargement of the pituitary, he drew attention to the work of some authors who made an analogy between pregnancy and temporary castration.

Post-partum Necrosis of the Anterior Pituitary

With regard to the pathological processes that occur in the pituitary, he wrote: "There occur in the hypophysis quite often, and definitely not as infrequently as some assume, various pathological processes leading to destruction of large areas of the glandular part which must necessarily affect gravely the functions of the hypophysis or even abolish them completely." He then described two cases of post-partum necrosis of the anterior pituitary.

The first case was that of a woman, aged 37, who had had two previous pregnancies, in each of which a craniotomy had had to be performed because of her narrow pelvis. In the third pregnancy a caesarean section was performed in an effort to deliver the child alive. Following atony of the uterus, she developed a severe post-partum haemorrhage and died from puerperal sepsis nine days after the operation. "Examination of the pituitary showed, apart from the usual changes seen in pregnancy, an extensive area of necrosis with a well-advanced proliferation of the connective tissue proceeding from the periphery and partial organization of the lesion. It was obvious that the necrotic changes must have existed for quite a time and they must have developed before childbirth. A case like this favours the hypothesis that an extensive necrosis leads to an endocrine disorder and causes atony of the uterus."

The second case was that of a woman, aged 33, who died from valvular disease of the heart six weeks after an abortion at six months. "Under microscopical examination an extensive necrosis was found in the glandular part of the pituitary, with secondary proliferation of connective tissue."

Glinski stated that the origin of these necrotic changes must undoubtedly be related to vascular thrombosis of the arteries supplying the pituitary.

He concluded one of his papers (Glinski, 1913d) with the following paragraph: "Parallel to these investigations [post-partum deaths] one should observe the state of the pituitary in every post-mortem examination, because even the changes of the hypophysis, which can be recognized at the present state of our knowledge, can, if correlated critically with exact clinical observations, yield information about many unknown facts regarding the physiology and pathology of the hypophysis. It is also quite obvious that parallel to these researches one must carry out studies in all directions, and should, during the investigation of the hypophysis, also take into account all the other endocrine glands."

Simmonds's Early Papers

These excellent observations of Glinski's in 1913 led me to consult again the early papers of Simmonds. He did not mention Glinski's work in his first paper (Simmonds, 1914a). In his second paper (1914b), he mentioned Glinski by name and wrote: "From foreign literature I only know through an abstract [Glinski, 1913b] the work of Glinski which had appeared in the Polish language. This author reports on two cases of puerperal sepsis, of which the first showed a purulent focus and the other a necrotic area in the pituitary. In the third case, he found, in a woman who had died six weeks after labour from cardiac disease, a circumscribed necrosis also within that organ. That is all that I found about this subject in the literature in spite of my greatest efforts."

Let us now return to Simmonds's first paper on the subject (Simmonds, 1914a). In reporting the case of a woman aged 46 he wrote:

"After the negative clinical findings we were rather interested in the results of the post-mortem examination. Nothing abnormal was found on the brain or the meninges. Apart from some thickening of the apical pleura and some pleural adhesions the lungs were normal. In the abdomen the small size of the liver, spleen, and ovaries was noticed. Their size corresponded to that usually found in an older woman.

"*I should like to stress that the histological examination of these organs, as well as of the pancreas, thyroid, kidneys, adrenals, and parathyroid glands, was completely negative.*

"The post-mortem examination would have left us in ignorance of the cause of death had I not finally removed the hypophysis and examined that organ. I noticed immediately the small size, softness, and abnormal appearance of the gland, which weighed only 0.3 g. I cut sections of the gland and examined them histologically. The result was surprising. Nothing was seen which could with certainty be described as the neural part, and of the pars intermedia there remained only a few colloid-containing cysts lined with ciliary epithelium. Of the glandular anterior lobe there remained only a few small strands and very few clusters of cells."

It was indeed a fortunate intuition that caused Simmonds to examine the pituitary gland in the absence of very abnormal findings in the abdomen macroscopically, and with completely negative histological findings in all the organs examined. In fact, it

was surprising that one of the most important and characteristic post-mortem findings in hypopituitarism should have escaped the attention of so critical an observer as Simmonds—namely, an atrophy of the endocrine glands such as the thyroid and the adrenals. It is true, as Sheehan and Summers (1949) have pointed out, that the changes are similar in type to those occurring after the menopause, and so a diagnostic significance may be difficult. But Simmonds's patient was only 46 years old; she had had the disease for eleven years, and in a very severe form, as practically the whole of the pituitary gland was destroyed. Fahr's case (1918), with less destruction of the anterior lobe than Simmonds's case, showed a marked atrophy of the adrenals, which weighed 1.4 g. and 1.6 g. (normal 10–15 g.).

A Characteristic Finding

Berblinger (1934) has stressed that a characteristic post-mortem finding in hypopituitarism is a generalized atrophy of organs and glands, and his findings in a man who had had the disease for seven years are worth recording:

	Case	*Normal*
Brain	1,120 g.	1,360 g.
Heart	230 „	370 „
Spleen	110 „	161 „
Liver	1,060 „	1,603 „
Kidneys	160 „	265 „
Pancreas	35 „	71 „
Adrenals	5 „	13 „
Thyroid	13 „	29 „
Testicles	6 „	36 „
Pituitary	0.2 g.	0.6 g.

Of the endocrine glands, the pancreas and thyroid have only half, the adrenals and pituitary one-third, and the testes only one-sixth of the normal average weight.

Histologically, these were Berblinger's findings:—adrenals: cortex and medulla narrowed; parathyroids: only clear principal cells, no oxyphil cells; thyroid: follicles mostly contain colloid, but epithelium low; pancreas: islets large; prostate: atrophy; epididymis: epithelium of the tubules present and normal, but no spermatozoa or cells in the lumen; testes: remarkably small; atrophy of tubules; interstitial cells do not contain fat or pigment. In the interstitium there were some fibroblasts and small-cell infiltration. In spite of a most careful examination no interstitial cells could be found. The wall of the arterioles showed lipoid change. There was therefore a diffuse severe atrophy of both testes with complete loss of spermatogenesis and absence of the typical interstitial cells which is typical of testicular atrophy due to hypophysial insufficiency.

Sheehan and Summers (1949) have described changes in the gonads and genital tract of the female analogous to that described by Berblinger in the male. In a later paper Cooke and Sheehan (1950) described detailed post-mortem findings in four cases. These cases showed an atrophy of most of the abdominal organs, and in the thyroid and adrenals in every case. One interesting observation they have recorded was the absence of atrophy of the parathyroid glands (in one case hypertrophy was present)—an unexpected finding if there is a parathyrotrophic hormone, but supported by normal values for serum calcium and phosphorus. These normal blood findings were also noted in a case presently under observation.

Conclusion

One can perhaps understand some difficulty in obtaining Polish medical journals and translations of the articles if the language is not known. This must have occurred to Glinski, for he published his third paper on "The Hypophysis in General and the Changes Occurring in Pregnancy in Particular" in German in a Berlin journal (1913d). This paper, in three parts, first appeared on June 16, 1913, and in the two subsequent weekly issues, or some six months before Simmonds gave his lecture at Vienna.

It is of interest to note that Glinski has also described tuberculosis of the pituitary in a child of 10 dying from generalized miliary tuberculosis in whom microscopical evidence indicated that the tuberculous inflammation spread into the pituitary by two different routes—by direct infiltration and by generalized miliary tuberculosis (Glinski, 1913a)—and also purulent changes in the pituitary due to meningococcal meningitis and puerperal sepsis (Glinski, 1913a).

Summary

This article has been written with the object of making Glinski's papers better known, as they do not appear to be generally available in this country. It is interesting to note that some 37 years ago Glinski advanced the hypothesis that necrosis of the anterior pituitary was the cause and not the effect of atony of the uterus, haemorrhage, and collapse in women at childbirth—a view subsequently elaborated by Taylor and Shea (1944), but not accepted by Sheehan (1948).

It is a pleasure to thank Dr. M. Frisch for assistance with the German translations.

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(With some notes on dates of their publication)

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In Korea the U.S. Army is using chloroquine as the standard malaria suppressant, and is hoping that, taken with primaquin, it will prove effective for all treatment. Various substances are also under test. "Physeptone" ("amidone") has proved effective in place of morphine; dextran, polyvinylpyrolidone (a plastic), and gelatin are under trial to replace plasma in transfusions; an iodoglobulin compound has been developed to sterilize water in the field instead of the usual chlorination. Actidione, a by-product in the manufacture of streptomycin, is a valuable rat repellent which may be used as a coating on the outside of packages and containers. For field use a sterile injection device contains helium under pressure, so that once the needle is in the skin a seal can be broken to let the gas force a drug into the tissues.

TWO CASES OF SIMMONDS'S DISEASE DUE TO POST-PARTUM NECROSIS OF THE PITUITARY GLAND

BY

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We report the following cases for several reasons. Every patient with Simmonds's disease presents a fascinating picture of deranged pituitary function which cannot be paralleled by operating on animals; the symptoms and response to treatment are very instructive from both the theoretical and the practical aspects. An important practical point is that the underlying pathology in these patients may not be suspected until many years of ill-health have elapsed, and it is probable that there are many more patients suffering from varying degrees of pituitary failure from this cause than are suspected. We feel very strongly that the title "Simmonds's disease" should be restricted to this type of case due to post-partum necrosis of the pituitary as described in Simmonds's original article.

Case 1

The patient, a married woman aged 42, had had ten normal pregnancies. Thirteen years previously the tenth pregnancy was followed by a severe post-partum haemorrhage. She was not admitted to hospital until 13 days after delivery, when she was transfused with 2 pints (1.14 litres) of blood. Lactation was not established, all pubic and axillary hair was lost, and no further menstrual period occurred. Her intelligence was low, and for many years she remained in a state of poor health without seeking medical advice. Six months before the present admission to hospital she went to her doctor because of "anaemia." She was admitted in January, 1949, for investigation of anaemia and weakness.

On examination she had a puffy mxyoedematous face, her skin was very dry, inelastic, and pale with a yellow tint suggesting carotinaemia. Her expression was dull and apathetic. Pubic and axillary hair was absent. Internal and external genitalia were atrophied. Her pulse was feeble, temperature subnormal, and blood pressure 90/? mm. Hg. She was not wasted.

Fig. 1 shows the more important investigations that were undertaken during the course of observation. Others were as follows. Kepler test, 23 (evidence of adrenal failure). Blood count after readmission (December 20, 1949): Hb. 60%; red cells, 3,700,000; white cells, 4,000 (polymorphs 58%, lymphocytes 34%, monocytes 6%, eosinophils 2%). Examination of urine and blood urea revealed nothing abnormal. E.C.G. showed normal tracings of low voltage. A radiograph of skull revealed nothing abnormal. A fractional test meal showed the presence of free hydrochloric acid.

The history and the physical examination rendered the diagnosis of Simmonds's syndrome almost certain, but two investigations were undertaken which confirm a diagnosis of anterior pituitary dysfunction—the determination of the 17-ketosteroids in the urine and the response to a test injection of insulin. The 17-ketosteroid result was confirmatory of the diagnosis, only a trace of this substance being found in the 24-hour specimen of urine. An insulin sensitivity test was then undertaken. As the condition of the patient was not very good, only one-third of the calculated dose of insulin—that is, 1¼ units—was injected intravenously. Within half an hour the patient felt faint, sweated, and

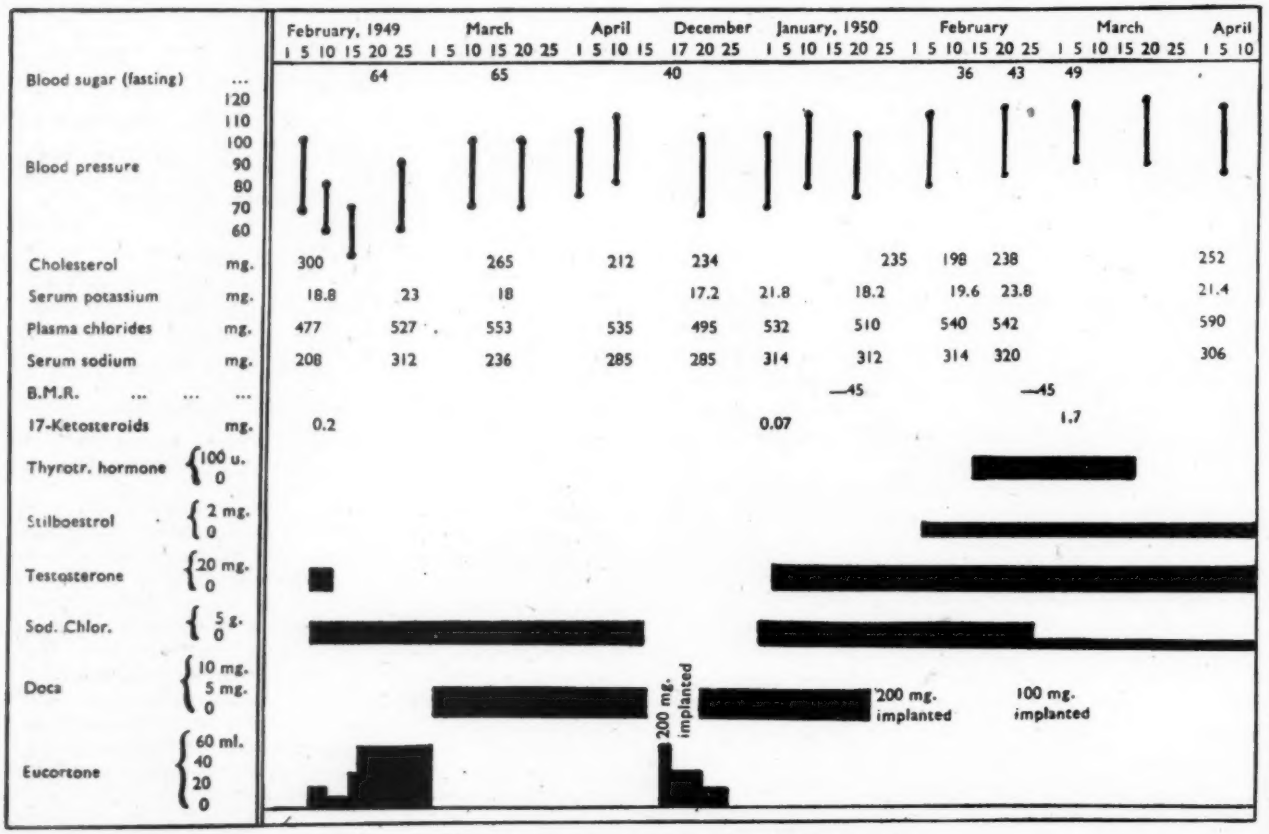

FIG. 1.—Case 1. Details of investigations and treatment.

became unconscious. The test was discontinued; the pulse was not perceptible, and the blood pressure fell to 60 mm. Hg.

Energetic treatment with glucose, adrenaline, and adrenal cortical extract ("eucortone") was started at once, but the patient remained semiconscious, confused, with a barely perceptible pulse and a systolic blood pressure between 60 and 74 mg. Hg for a fortnight. The blood-sugar figures were as follows: fasting, 33 mg. per 100 ml.; 5 minutes after insulin injection, 31 mg.; 15 minutes, 17 mg.; 30 minutes, 22 mg. No further samples were taken owing to the serious condition of the patient. Unfortunately the test dose of insulin was given before the results of the fasting blood sugar had been received from the laboratory, otherwise the test would not have been undertaken.

The treatment is recorded in Fig. 1. It will be seen that for the first few days, owing to lack of supplies, the dose of eucortone was only 10–20 ml. daily; thereafter it was raised to 60 ml. A few injections of testosterone propionate were given, but these had to be discontinued because they induced restlessness. Thyroid gland (dry) 1/5 gr. (13 mg.) was tried on three successive days, but caused diarrhoea and a fall of blood pressure, so it could not be continued. The patient improved gradually, and at the beginning of March treatment with "doca" was substituted for eucortone, and later 200 mg. of doca was implanted and the patient was discharged in fairly good condition taking 5 g. of salt extra, with 10 mg. of methyl testosterone sublingually, which now had no ill effect. When seen in the out-patient department one month after discharge she was well; thereafter she ceased attendance.

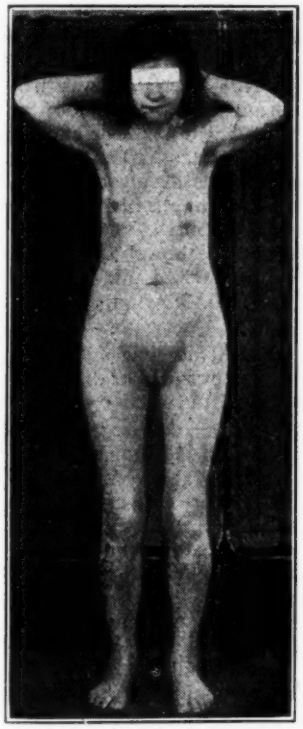

Fig. 2.—Case 1. Photograph showing absence of axillary and pubic hair and poor mammary development.

The patient was readmitted in December, 1949, unconscious; no history was obtainable. The pulse and blood pressure were imperceptible. A vein was exposed; no blood could be obtained, but a glucose–saline drip was given with intravenous injections of 10 ml. of eucortone every four hours. She regained consciousness in a few hours and gradually improved. In January, 1950, 200 mg. of doca was implanted, and in March 100 mg. As the patient could not tolerate thyroid gland, thyrotropic hormone was given in doses of 200 units every other day for five weeks; the only changes noticed were that the skin became less dry and the hair of the head improved in appearance.

The patient was discharged in March, 1950. The myxoedematous appearance had not changed, and the skin remained dry. She was anaemic; iron had not been well tolerated, and difficult veins precluded the use of iron intravenously. Since discharge she has remained well, and has been able to do some housework and shopping. The raising of the haemoglobin level still remains a problem.

Case 2

The patient, a married woman aged 48, had had five pregnancies between 22 and 17 years previously. A postpartum haemorrhage occurred after the second and fifth pregnancies. Amenorrhoea has been present since the last pregnancy, and since then she has never felt quite well. She has attended the doctor for the last five years on account of "gastric complaints" and "anaemia." She was admitted to hospital on August 27, 1949, in a semi-comatose condition, into which she had lapsed three days before.

On examination she was mentally confused; her face was myxoedematous, her skin was dry and pale, the hair of the scalp was dry, and pubic and axillary hair and eyebrows were missing. Internal and external genitalia were atrophied. Petechiae were present on shoulders and ankles. The patient was not wasted. Her temperature and pulse were subnormal. Her blood pressure was 90/55 mm. Hg. A blood count showed: Hb, 90% (red cell count not done); white cells, 5,300 (polymorphs, 58%, lymphocytes 34%, monocytes 5%, eosinophils 2%, basophils 1%); blood urea, 19 mg. per 100 ml.; blood sugar, 62 mg. per 100 ml.; serum chloride, 565 mg. per 100 ml.; serum sodium, 334 mg. per 100 ml. The urine was normal. An E.C.G. showed normal tracings of low voltage.

The mental symptoms and stupor suggested hypoglycaemia; intravenous glucose brought an improvement, but mental confusion persisted. Further consideration suggested the diagnosis of Simmonds's disease because of the history and the physical resemblance to Case 1. Eucortone, 5 ml. daily, was given and the confusion cleared at once, and the general condition thereafter improved. Estimation of 17-ketosteroids in the urine showed only 0.5 mg. for 24 hours, confirming the diagnosis. In view of the previous experience the insulin tolerance test was not done. Thyroid gland, ½ gr. (32 mg.), was given twice, but this small dose was not tolerated; the blood pressure fell to 80/60 mm. Hg. and that treatment was discontinued. Subsequently the patient improved gradually on an extra 5 g. of salt, with 10 mg. of methyl testosterone sublingually. On discharge in November, 1949, she still looked myxoedematous, but was able to do light work. Since then she has been living a normal life and her health has been maintained by implants of doca and methyl testosterone sublingually.

Interesting Points Resulting from the Chemical Investigations

In Case 1 the blood cholesterol was high owing to secondary myxoedema, but fell during treatment. The sodium and chlorides were at first low, improved on treatment with salt and doca to normal level, and had to be restricted later owing to development of oedema. The potassium level was normal. Total serum protein (Case 1) was normal, but the A./G. ratio was reversed: albumin 2.5%, globulin 3.8%. This is unexplained. Hypochromic anaemia was present, the eosinophils were 1%, 2%, and *nil* in three counts. This type of anaemia is also found in hypothyroidism, and is noted by Escamella and Lisser in a number of verified cases. All blood-sugar estimates were low. It is interesting to note that the ketosteroid estimation rose after treatment.

Comment

The interest of these patients lies in the fact that the pituitary gland had been so seriously disturbed that the production of thyrotropic, gonadotrophic, and adrenocorticotropic hormones was severely reduced. They both showed features of myxoedema with subnormal temperature, slow pulse rate, intolerance to cold, and lowered B.M.R. The lack of gonadotrophic influence was shown by the cessation of menstrual periods at an early age, the subsequent sexual involution, and the absence of sexual hair. The lack of adrenocortical hormone was shown by the low blood pressure, low blood-sugar level, and by the low ketosteroid production. With

such severe damage treatment is necessarily difficult. It has been found that pituitary extracts are of no value.

The great value of adrenal cortical extract and salt was conclusively shown by our patients. Certainly Case 1 and probably Case 2 would have died without it. In the first patient the injection of insulin precipitated an adrenal crisis, on the verge of which she must have been living for a long time. This test illustrated only too clearly the danger of giving a dose of insulin in patients with severe degrees of pituitary failure. If the diagnosis can be made without the test it is clearly much safer not to do the latter. In Case 2 there was the same underlying mechanism, though not so severe. Both patients recovered a fair degree of health with adrenal cortical hormone and later doca. It was possible to substitute doca implants for the whole adrenal extract, provided sufficient was implanted. This suggests that doca must have more widespread action than just the regulation of sodium and potassium balance, which in these patients was not grossly upset so far as the chemical investigations show. The level of the blood sugar was not raised by treatment.

Most of the more recently reported cases have been treated mainly with testosterone by mouth, injection, or implant; the very good effect of doca in our patients is worth stressing. In patients with secondary myxoedema it has been previously noted that thyroid gland may not be tolerated. This was the case in our patients, and patients who show signs suggesting myxoedema should be examined for other signs of pituitary hypofunction before thyroid gland is given. As in the case of insulin, thyroid gland may be a dangerous drug in these patients even in a very small dose, and should be given with great caution. It had a very adverse effect with both patients. It is to be noted that adequate blood transfusion for treatment for the initial post-partum haemorrhage had not been given. In Case 1 a small transfusion was given 13 days after the haemorrhage. In Case 2 no blood was administered. It would seem likely that adequate prompt transfusion of such cases would prevent the development of this sequel.

Summary

Two patients with characteristic history and physical signs of anterior pituitary gland failure following post-partum necrosis of the gland are presented.

Both showed symptoms of adrenal crisis and responded to treatment by adrenal extract and salt. Both are being maintained in fair health by implants of doca and methyl testosterone by mouth.

On April 16 Professor E. J. Cohn, of Harvard University, demonstrated at Cornell University Medical School an interesting machine which processes blood as fast as it is drawn from the donor, according to a *New York Times* report. The machine, which is portable, made of plastic materials, and can be sterilized, prepares plasma at the rate of 0.5 ml./sec., or over three pints an hour. Blood flows direct from the vein over an exchange resin, which removes calcium and so prevents clotting, is then cooled, and passes into a small continuously running centrifuge which separates cells and plasma. Prothrombin is then removed from the plasma by a second resin which absorbs it, and a zinc glycine solution is added to precipitate fibrinogen and gamma globulins, which are centrifuged off. The remaining plasma protein (largely albumin), after removal of the zinc, is frozen, sterilized by exposure to an electron beam, and is then ready for storage or use.

Medical Memoranda

Phlegmonous Enteritis Occurring After Strangulated Femoral Hernia

This unusual sequela of a strangulated hernia seems to be worthy of record.

Case Report

A married woman aged 40 was admitted to hospital on May 4, 1950, as a case of strangulated femoral hernia of six hours' duration. She had vomited twice and was experiencing colicky abdominal pain. Clinical examination at the time of admission confirmed the presence of a tender irreducible right femoral hernia. The abdomen was slightly distended and auscultation revealed hyperactive peristalsis. Operation was undertaken within two hours of admission.

First Operation.—A Lotheissen-type operation was performed. The sac contained a firmly incarcerated loop of small bowel, the upward delivery of which could be effected only after division of Gimbernat's ligament. The affected bowel, 1–2 in. (2.5–5 cm.) in length, was deeply congested, but, following delivery from the sac, on application of a hot swab it rapidly regained its normal colour. Normal lustre and contractability were present, and the bowel accordingly was adjudged viable. The sac was excised and a repair effected with interrupted sutures of No. 7 nylon.

The patient made an uninterrupted recovery and was discharged from hospital on May 18. At no time during her stay in hospital was there any complaint of pain or diarrhoea, and no evidence of incipient intestinal obstruction.

On May 19—that is, the day after her discharge home—she was readmitted with a history of 14 hours' central abdominal pain accompanied by nausea and vomiting. On admission she was obviously ill. Her temperature was 99.5° F. (37.5° C.) and the pulse rate 110. Her tongue was dry and furred. Abdominal examination showed slight generalized distension with rebound tenderness and guarding in the central abdominal zone and in the right iliac fossa. Auscultation showed hyperactive peristalsis. Rectal examination gave no useful information. A diagnosis of intestinal obstruction was made, and laparotomy was performed some two hours after admission.

Second Operation.—On May 19 the abdomen was opened through a lower right paramedian incision, a quantity of clear straw-coloured fluid escaping on opening the peritoneal cavity. At about 2 ft. (61 cm.) from the ileo-caecal junction a segment of ileum, presumably that portion of the bowel which had previously been incarcerated in the femoral hernial sac, was found to be the site of a phlegmonous induration. The portion of gut affected was some 4–6 in. (10–15 cm.) in length, almost twice the length of the gut originally incarcerated in the hernial sac. Its colour was dusky red and it was mottled in appearance. It was considerably thickened and rubbery in consistence. The adjacent mesentery was oedematous and palpably thickened. The area was fairly sharply demarcated from normal ileum, which was collapsed distal to and moderately distended proximal to the lesion. An interesting feature was the complete absence of any plastic peritonitis such as might have been expected under such conditions. A diagnosis of localized phlegmonous enteritis was made, and about 20 in. (50 cm.) of bowel was resected. Continuity was restored by a side-to-side anastomosis and the abdomen closed without drainage.

After operation the patient developed paralytic ileus, which necessitated the use of continuous aspiration and intravenous saline therapy for five days. Bowel function returned normally on the seventh day, and she then had a protracted but

satisfactory convalescence. A pelvic abscess developed, but it burst spontaneously per rectum on the fourteenth post-operative day. She was eventually discharged from hospital on June 30.

The Specimen.—When opened, the resected bowel presented the following features: (1) The normal mucosal pattern was replaced by a grossly distorted and oedematous appearance. This oedema had considerably reduced the calibre of the lumen of the bowel. (2) The muscular coat was swollen with oedema to almost twice its normal thickness, but there was no evidence of loss of continuity or of commencing perforation of the bowel. (3) There was evidence of patchy submucosal haemorrhage with one or two ragged areas of apparent mucosal erosion.

Comment

It is interesting to speculate on the probable pathogenesis of this condition. Judged by all the accepted standards, at the time of the original operation the incarcerated portion of ileum was viable. Non-viability of a portion of the gut wall would inevitably have been followed by a perforation or the formation of a localized abscess. The absence of both these complications precludes the possibility of permanent ischaemic changes in the bowel having been overlooked. Viability, as judged by the external appearance of the bowel, however, does not exclude the possibility of a varying degree of mucosal necrosis.

Paget (1879) taught in his lectures on strangulated femoral hernia that, "short of gangrene, there may be ulceration of the mucosa of the intestine." Barry (1942), in a comprehensive review of intestinal stricture following strangulated femoral herniae, reiterated this point, and conjectured that cicatricial contraction arising as a result of permanent damage to the mucosa is the main causative agent in the production of obstruction.

The gross appearances of the affected segment in this case, however, were those of an acute localized phlegmon of the ileum. It is most likely that this arose as a result of infection reaching the submucous zone through the damaged and ulcerated mucous membrane of the incarcerated bowel, the causative agent in all probability being a streptococcus.

James (1942), reporting a case of localized phlegmon of the jejunum, stated that areas of suppuration in the gut wall were a common feature in this condition, though none was noted here.

The appearance of the bowel was not unlike that of Crohn's disease, except that the mesentery was not as extensively involved and there was no evidence of enlarged lymph nodes. This similarity in appearance to Crohn's disease was also remarked upon by Barry (1942) in the first of the three cases he reported. The similarity of the gross appearance of the bowel to that of Crohn's disease suggests the possibility of a common aetiology—namely, that the latter disease results from chronic inflammation of the bowel wall of enterogenous origin.

I wish to thank Professor R. St. Leger Brockman for permission to treat and record this case.

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Bladder Loculus Simulating Strangulated Inguinal Hernia

The following case seems to be of sufficient rarity and interest to merit recording.

Case Report

A negro aged 32 was admitted to hospital with a painful swelling in the right groin which he was said to have had for two weeks. He could not speak English, and no other accurate history was available. An impression, however, was gained that he had had some vomiting but no constipation.

The swelling had the characteristics of an irreducible inguinal hernia. The question of strangulation could not be excluded with certainty, and it was decided to explore the swelling immediately.

At operation a large mass was found in the inguinal canal and scrotum from which a medium-sized indirect hernial sac was excised after having been found to be empty. This completed, there remained the large mass still occupying the canal and scrotum; it was covered with fibrous tissue. During the examination it was opened and found to be hollow, with muscular walls, and to contain a liquid immediately suggestive of urine. Further exploration within this cavity confirmed that it was in fact a large loculus of a bilocular bladder. In the absence of information about the site of the right ureter and relative sizes of the two loculi it was decided to defer excision of the loculus, should this be feasible, until further investigation had been made. The opening in the bladder was closed, the wound drained, and a penile catheter inserted.

He made a satisfactory recovery, and four weeks later the large loculus was excised by Mr. A. Kirk Wilson uneventfully.

Comment

The absence of an adequate history in this case added to the diagnostic difficulty, and it is doubtful whether, without any definite relationship between the inguinal swelling and urinary symptoms, an accurate pre-operative diagnosis could have been made. It is unfortunate that the language barrier prevented any urinary history from being obtained, even after operation. Although the bladder should be suspected as being a part of any inguinal swelling, the large size of this—it reached and filled the scrotum—made its presence unlikely.

This bilocular bladder could be regarded as the para-peritoneal type of Wakeley (1939), though those discussed in his article dealt with only relatively small protrusions.

A case presenting many similar features was described by Stock (1947). In his case the patient was an African negro, and not until the bladder loculus was opened was a diagnosis made; the loculus was smaller, however, and was excised immediately.

R. A. C. OWEN, F.R.C.S.

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King Edward's Hospital Fund for London is to open a School for Hospital Catering at St. Pancras Hospital towards the end of May. The aim will be to illustrate new methods and ideas, and all aspects of catering will be covered. Four full-time courses, both refresher and basic, ranging from 10 days to eight weeks, will be run for roughly 30 students who are already employed in hospital catering.

Reviews

HISTORY OF MEDICINE IN PERSIA

A Medical History of Persia and the Eastern Caliphate from the Earliest Times until the Year A.D. 1932. By Cyril Elgood, M.A., M.D., F.R.C.P. (Pp. 617 ; 7 figures. £2 10s.) Cambridge: The University Press. 1951.

Dr. Elgood's fine book is in a grand literary tradition, of which the best-known exponent was James Morier (1780–1849), who died just over a century ago. His classic *Hajji Baba of Ispahan* (1824) is still read with delight by multitudes. Dr. Elgood, like Morier, was on the staff of the British Legation to Persia and, like him, writes from much first-hand knowledge.

No existing civilization is more ancient than the Persian. In the third millennium B.C. it was from Persia that the Indo-European invaders of India descended into that sub-continent. In the seventh century B.C. Persia produced a lofty ethical religion, associated with the name of Zoroaster, of which there are still remnants in outlying parts of Persia and in more vigorous state among the Parsees of Bombay. In the next fifteen hundred years the Persian Empire was great and powerful. Persian influence in religion, in magic—that word is Persian—and in art affected the Eastern Mediterranean in the late pre-Christian and early Christian centuries, and is visible in the New Testament and in some later books of the Old. The Persian Empire was for long a threat to Rome and to its eastern successor, New Rome, Byzantium, or, as we now call it, Constantinople. Most of the ancient civilization of Persia was swept away by the Arab conquest of the seventh century, the Mongol conquest of the thirteenth, and the Turkish of later times. It is astonishing that the Persian language and, to some extent, Persian customs have persisted through these changes. All this forms the necessary background of this work, and Dr. Elgood tells it admirably. He is not responsible for the inevitable fact that the enormous background encroaches upon the stage itself. This is altogether necessary for the intelligibility of the extremely intricate story that he has to tell.

Among the many interesting points here raised we can refer only to a very small proportion. The idea of sickness as due to possession by devils reached the writers of the New Testament from Persian sources. The origin of hospitals has always been a much disputed point ; Dr. Elgood shows that there is evidence that the form which they took was influenced by Persia. The earliest hospital pharmacopoeia of which we know was Persian and of the twelfth century. It is possible that the operation of couching for cataract may be of Persian origin. With the rise of Arabic as a *lingua franca* the use of Persian for scientific purposes lapsed, but some of the greatest physicians who used Arabic were Persians and nearly all of the Eastern Caliphate. Among these were Rhazes (860–930), of Basra, the greatest of the early chemists, who gave the first description of measles and of whooping-cough, and Avicenna (980–1036), of Bokhara, whose *Canon* was the most widely read text-book ever written. A claim might be made for Persia as the home of the earliest modern anatomical illustrations, and perhaps of the earliest modern attempt at practical anatomy on the bodies of apes. One of the ablest and most readable sections of Dr. Elgood's book describes the impact of Western Medicine on Persia from the seventeenth century onward. This section, which contains much original work, would in itself have made the book well worth writing.

All this is to the good in a remarkable record. But the reviewer cannot recall a more nauseating account of cruelty and wickedness persisted in through ages than that here set forth. Dr. Elgood is bound by facts and the tale had to be told, but it needs a strong stomach if some of it is to be visualized. We wish Dr. Elgood had included a few maps and chronological tables to illuminate a narrative that is necessarily extremely intricate and sometimes, therefore, a little difficult to follow, however well expounded.

CHARLES SINGER.

PATHOLOGY IN MAN

Allgemeine Pathologie. By Professor Franz Büchner. (Pp. 528 ; 424 figures. M. 32.80.) Munich and Berlin: Urban and Schwarzenberg. 1950.

Professor Büchner's teaching has been known—though imperfectly—for many years through the notebooks of his students. In this work, which took eight years to write, great experience and wide philosophical culture have combined to produce a highly original presentation of pathology. It is in fact a synthesis of pathological knowledge obtained by all techniques and is accordingly an important contribution to the teaching of the subject. The book is unique in its scope and comprehensiveness ; and, while the author lingers longest on what all pathologists will regard as common ground, he takes the freedom of Plato to contemplate all time and existence. In so doing, he illustrates the truth of H. R. Dean's bold assertion that "to a pathologist, all things are pathology." But he does more : he vindicates it both philosophically and historically, for this book is no chance phenomenon, but the logical development of ideas latent in Virchow.

Büchner holds that three great questions should dominate the thinking of a doctor : the nature of life, the nature of illness, and the nature of man. This conviction gives the book its tone and direction ; it also provides the three cardinal themes of the introduction. The first of these is an account of biological philosophy from Democritus to Driesch ; the second is an equally excellent history of pathological thought from Hippocrates to Virchow, whose genius gave pathology a form that in all essentials is current to-day ; the third is a discourse on the nature of man, which recognizes his uniqueness as a self-conscious organism, and by implication condemns as incomplete any account of pathology that ignores mind and the subtle and perpetual interplay of mental and physical factors in disease.

Büchner's work is not simply functional pathology : it is at once more profound and more imaginative ; all branches of pathology—morphology, chemical pathology, abnormal physiology, and psychopathology—are treated as sciences worthy of assiduous study for their own sakes : and one of Büchner's main objects (to use his own expression) is to make morphology speak. The subject matter of Büchner's book is as familiar outside Germany as within, but the teaching of it is normally shared by a variety of specialists not necessarily interested in each other's work. The distinctive character of this book derives from the author's sympathetic insight into a group of special disciplines and his ability to integrate their achievements.

The historical introduction is followed by a short account of pathological changes in the nucleus and

cytoplasm, and by a comprehensive discussion of abnormal metabolism and of the main disorders of respiration, circulation, blood pressure, growth, and development; this section also includes accounts of neoplasia, inflammation, and endocrine disorders. The next section is on heredity and environment in relation to disease, and includes discussions of physical agencies and vitamin deficiencies as causes of disease, chronic granulomas, and occupational diseases; it also contains an outline of meteoropathology—the weather in relation to disease. The final section is devoted to psychosomatic diseases and ends with a description of the growth and decay of what William McDougall would have termed a sentiment of love. The illustrations, printing, paper, and binding are all of the best quality and worthy of the Freiburg school of pathology.

The philosophical-historical approach to a science is probably easy and congenial to German students. Most British students find it difficult, and pathologists who try it usually revert to the traditional British method—unphilosophical, matter-of-fact descriptions of phenomena. Outside Germany, Büchner's work is most likely to appeal to practitioners of some experience—physicians and surgeons as well as pathologists—and also to biologists interested in medicine. Those who read it will find the author revealed as a true son of Aesculapius—modest and lovable as well as learned, and deeply devoted both to medicine and to his students.

RAYMOND WHITEHEAD

STERILITY

La Stérilité Involontaire. Evaluation des Méthodes de Diagnostic et de Traitement. By R. Palmer, with the collaboration of Mme. E. Palmer. (Pp. 492; illustrated. 1,600 francs.) Paris: Masson et Cie. 1950.

It seems a pity that this book is paper-backed and that its first perusal necessitates much tiring surgery with a paper-knife, for it contains such an amount of information that it deserves a permanent place in the library of all those concerned with the clinical aspects of human infertility. The illustrations, except for a few photomicrographs, are simple line drawings. While acknowledging opinions old and new, the author mainly gives an account of the views, experience, and practice of himself and his associates; the techniques and instruments developed in his clinic are naturally given prominence. Thus coelioscopy, which Dr. Palmer was the first to apply to the study of sterility in the female, is championed against culdoscopy. Certainly his claim that preliminary coelioscopy is of value in assessing whether a reconstructive operation on the tubes is likely to be successful merits careful consideration.

After a short account of the relevant normal physiology in both sexes, there is a full discussion of diagnostic procedures, including hormone assays, and the possible sources of error in their application. The final section is on the various aetiological factors individually, their diagnosis, and an evaluation of the methods of treatment available. A meticulous attention to detail is evident, but the broad outlook on the problem of the infertile couple is never lost sight of. The personal presentation of the material naturally invites disagreement on some points, but the book's graphic style makes it eminently readable, while the bibliography, with its many references to the Continental literature, will be found very useful.

S. BENDER.

EYES AT WORK

Eyes in Industry. A Comprehensive Book on Eyesight written for Industrial Workers. By Dorothy Adams Campbell, M.A., M.B., B.S., W. J. B. Riddell, M.D., F.R.S.Ed., F.R.F.P.S., and Sir Arthur Salusbury MacNalty, K.C.B., M.A., M.D., F.R.C.P., F.R.C.S., Hon. F.R.S.Ed. Preface by Lord McGowan, K.B.E., D.C.L., LL.D. Introduction by Sir Stewart Duke-Elder, K.C.V.O., D.Sc., Ph.D., M.D., F.R.C.S. (Pp. 234; illustrated. £1 10s.) London: Longmans, Green and Co. 1951.

This book, which is in three parts, covers the major factors concerned in the care of the eyes and the prevention of eyestrain and disease in industry. In the first part Dr. Campbell describes the structure and function of the eye and the conditions which influence sight. Professor Riddell in the second part describes the nature of the eye injuries and the risks to which both agricultural and industrial workers are liable. In the third part Sir Arthur MacNalty is concerned with industrial injuries from the administrative and public health points of view. In addition there is a preface by Lord McGowan and an illuminating introduction of some length by Sir Stewart Duke-Elder.

The book is written for the industrial worker in clear and simple language. Only in one place did the reviewer find that this was carried to an extreme—namely, calling the space behind the lens the posterior chamber. The part of the book headed "Eyesight and Work" includes chapters on the structure and function of the eye, movements of the eye and binocular vision, nutrition of the eye, preparation for industry, adolescent eyesight, visual requirements in industry, eye defects common in adults, illumination, and aids to vision. The second part, on visual hazards in industry and their prevention, includes material on agricultural and industrial hazards, prevention and first aid, and blind and partially sighted workers. Sir Arthur MacNalty discusses special aspects of industrial eye injuries and the psychology of sight. There are four appendices: the first-aid treatment of eye injuries, a schedule of recommended values of illumination, visual standards in industry, and a model form of certificate of blindness.

This is a comprehensive work. It is well illustrated and does all it sets out to do. It is a welcome addition to ophthalmic literature.

EUGENE WOLFF.

BOOKS RECEIVED

Review is not precluded by notice here of books recently received

Bentley and Driver's Textbook of Pharmaceutical Chemistry. Revised by J. E. Driver, M.A., Ph.D., M.Sc., F.R.I.C. 5th ed. (Pp. 671. 32s. 6d.) London: Geoffrey Cumberlege. 1951.

The Chordates. By H. W. Rand, Ph.D. (Pp. 862. 45s.) London: H. K. Lewis. 1950.

The Neurologic Examination. By R. N. DeJong, M.D. (Pp. 1,079. 110s.) London: Cassell. 1951.

The Encircled Heart. By J. Elder. (Pp. 271. 8s. 6d.) London: Lutterworth Press. 1951.

The Order of the Court. By J. D. Pank. (Pp. 191. 8s. 6d.) London: Hodder and Stoughton. 1951.

Animal Evolution. By G. S. Carter. (Pp. 368. 30s.) London: Sidgwick and Jackson. 1951.

The Biochemistry of Fish. Edited by R. T. Williams. (Pp. 105. 12s.) London: Cambridge University Press. 1951.

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INDUSTRIAL REHABILITATION

It is now seven years since the inter-departmental committee on the rehabilitation and resettlement of disabled persons (the Tomlinson Committee) issued its report and recommendations which preceded the passing of the Disabled Persons (Employment) Act of 1944. Under Section 3 of this Act the Minister of Labour is empowered to provide "industrial rehabilitation courses" for persons who by reason of unfitness arising from injury, disease, or deformity are in need of vocational training. Since the Ministry's pioneer industrial rehabilitation unit (I.R.U.) was opened at Egham in 1944 much valuable experience has been gained, and the results have been so encouraging as to warrant the establishment of 12 additional units. These units are run in affiliation with Government training centres (G.T.C.s) at Birmingham, Cardiff, Coventry, Edinburgh, Felling-on-Tyne, Glasgow, Hull, Leeds, Leicester, Long Eaton, Manchester, and Sheffield. Each unit, together with an additional one recently opened at Bristol, has accommodation for upwards of 100 persons of either sex, but with the exception of Egham, which can take 180, they are non-residential. They are well equipped with workshops, gardens, gymnasia, and canteens, and are staffed by trained and experienced workers.

The type of patient most in need of rehabilitation has usually had a severe injury or illness resulting in a marked reduction in working capacity, with loss of self-confidence. For such cases progressive reablement or vocational training in the event of permanent incapacity is of the utmost importance after discharge from hospital. In planning such a course at an I.R.U. the staff are guided by recommendations from either the private doctor or the hospital, and individual requirements will vary according to the physical condition, temperament, and aptitude of the person concerned. The courses at the units have two chief aims—to restore confidence, both mentally and physically, by a gradual adjustment to working conditions, and to assess the suitability for selected types of work. The treatment consists in the main of graduated exercises of a remedial nature in combination with gymnastics, physiotherapy, and occupational therapy, the latter carried out in an atmosphere akin to that of industry itself, and with emphasis placed on real productive work rather than on the orthodox handicraft methods of the occupational therapist. Where aptitude is discovered for a skilled trade arrangements can be made for the patient to be transferred to a Government training centre for the necessary training to be given under the Ministry's vocational training scheme. The average time spent in an I.R.U. is 6–7 weeks, but if need be this can be extended to 12 weeks. Each unit is under the control of the manager of the G.T.C., and the staff includes a rehabilitation officer with industrial and administrative ability, a vocational psychologist, a social worker, a chief occupational supervisor, and a disablement resettlement officer (D.R.O.).

A total of 13,213 persons have passed through these centres since the inception of the scheme, and 66% of these were referred by general practitioners or by hospitals. The remaining 44% were offered industrial rehabilitation at local offices of the Ministry of Labour through the D.R.O., who is concerned with the placing in suitable employment of all those who have passed through the unit and of others with a permanent physical handicap. The D.R.O. has special training for his work, and he is always available to interview in private a disabled person who applies for assistance at the employment exchange, where he is informed of all vacancies notified by local employers, with whom he keeps in close touch. He is also available at the medical interviewing committees which have been set up at selected hospitals to assist in finding the right work for the seriously disabled. A simple recommendation by a doctor to the employment exchange that his patient is in need of industrial rehabilitation is all that is necessary to enable the local D.R.O. to apply for a vacancy in the nearest industrial rehabilitation unit. After a job has been found for a patient who has been through a rehabilitation course the D.R.O. follows the case up in order to ensure that resettlement is successful. Over 80% of persons who have completed a course have been satisfactorily placed, 14% of these having received training in a skilled trade under the Ministry's vocational training scheme. Any person over the age of 16 is eligible, and maintenance allowances on a graduated scale, depending on domestic and family circumstances, are payable, free from tax, while training is being taken. Similar

1 *Ministry of Labour Gazette*, May, 1950. See also annotation in the *British Medical Journal*, 1951, 1, 518.
2 Napier, J. R., Barron, J. N., Gregory, T. P., and Thompson, D. R., *British Medical Journal*, 1947, 2, 203.
3 Plewes, L. W., Barron, J. N., Thompson, A. R., and Hewell, H. H., *Lancet*, 1948, 2, 699.
4 Thompson, A. R., *Brit. J. phys. Med.*, 1949, 12, 114.
5 Thompson, A. R., in *Recent Advances in Physical Medicine*, edited by Bach, F., 1950, London, pp. 403–22; 440–8.

facilities for the blind are available at the Ministry's residential centre at America Lodge, Torquay.[1]

Of no less interest is the part now being played by some of the larger industrial undertakings in the rehabilitation of their own workers.[2-5] Here the physical and psychological rehabilitation of employees injured at work or elsewhere, as well as those who are disabled by disease, is shared between the rehabilitation department of the hospital and the remedial workshop set up in the factory itself. In such factories the place of the D.R.O. is taken by a rehabilitation superintendent with an engineering and industrial background, who acts as the liaison officer between the hospital and the factory, working under the direction of the industrial medical officer. Such a project, however, requires close co-operation between the industrial medical department and the hospital, supported by an enlightened general-practitioner and consultant service and by a management prepared, under suitable guidance, to place the resources of industry at the disposal of the medical profession. The results achieved have been very encouraging and suggest that for most types of injury, whether encountered in industry or elsewhere, engineering methods can go a long way in replacing the conventional type of occupational therapy in the restoration of function within the patient's own working environment.

ULTRASONICS IN DIAGNOSIS AND THERAPY

Although ultrasonics were first tried in medicine about 1927 it is only in the last three years that there has been a flood of papers on the subject, principally from Austrian and German workers, to which the reports of the international congresses held at Erlangen in 1949 and Rome in 1950[1] provide some guide. Sound or sonic energy is a form of mechanical energy transmitted through matter as vibrations or propagated waves. Particles of matter are displaced back and forth longitudinally in the medium, producing in it alternating zones of pressure and rarefaction. If the frequency of vibration is above 20,000 cycles per second this energy is called ultrasonic. For medical purposes frequencies from 800 to 3,000 kilocycles per second are generally used, produced from quartz crystal oscillators. This makes use of the so-called piezoelectric effect shown by certain crystals, which when placed in an alternating electric field proceed to change shape (i.e., to oscillate) with the same frequency as the field, and thus to produce high-frequency vibrations. Similarly, a magnetized rod held in an alternating magnetic field is set into vibration by the field and emits ultrasonic vibrations from its ends. This magnetostrictor, as it is called, produces ultrasonics of higher energy but lower frequency than the quartz oscillator.

The biological effects of ultrasonics have been extensively studied, and varying conclusions have been reached. It is, however, generally recognized that the principal effects on living tissues are mechanical, thermal, and chemical. In therapeutics mechanical and thermal effects are probably of equal importance, chemical effects being difficult to assess outside the laboratory. The best picture of the mechanical effect seems to be that put forward by von Sanden.[2] He compares it to the result of shaking a sieve full of stones. The stones will pass through the mesh during agitation but not if the sieve is held still. Similarly the rate of diffusion through semi-permeable membranes in the tissues under the influence of normal osmotic and hydrostatic pressures is greatly increased by the agitation of the ultrasonic field. The thermal effect is greatest at interfaces between tissue layers, as at fascial planes, joint capsules, and the periosteum of bone. In this way heating by ultrasonics differs from that of the various forms of diathermy and microwaves. The combined result of thermal and mechanical effects is therefore hyperaemia and greatly increased exchange of tissue fluids, with consequent increase of local metabolism. Chemically the acceleration of oxidative processes is probably the main effect.

Many other phenomena are known in laboratory practice and have been used in industry—for instance, the detection of flaws in metals by the reflection of ultrasonic beams. Gross destructive effects, due to heating and to the phenomenon of cavitation, with splitting and fragmentation of tissues, can be produced in plants and animals but require much higher energies than those normally used in ultrasonic therapy.

Thus the logical application of ultrasonic energy in treatment seems to be in the promotion of local inflammatory reactions and particularly the softening, by hyperaemia and diffusion, of fibrous tissue deposits. Analgesic and spasmolytic effects have repeatedly been observed in the treatment of muscle and nerve lesions and there is evidence of peripheral autonomic effects when ganglia are exposed to the ultrasonic beam.

1 *Der Ultraschall in der Medizin*, 1950, **2**. Edited by K. Woeber. S. Hirzel Verlag, Zurich. Contains a list of 678 articles on the subject in various journals.
2 *Practice of Ultrasonic Therapy*. G. Barth and K. von Sanden. Translated from *Aerztliche Praxis*, 1950, **2**, 9, 11, 21, 29, 30. Siemens, Ltd.
3 *Archives of Physical Medicine*, 1950, **31**, 6. See also *American Yearbook of Physical Medicine and Rehabilitation*, 1950, and the international review section of *Occupational Therapy and Rehabilitation*.
4 *British Medical Journal*, 1950, **2**, 1107.
5 Wild, J. J., and Neal, D., *Lancet*, 1951, **1**, 655.
6 Ballantine, H. T., Holt, R. H., and others, *Science*, 1950, **112**, 525.

Inflammatory conditions treated successfully include acute and chronic skin lesions, in particular chronic ulcers and sinuses. Localized sclerodermatous infiltration and Dupuytren's contracture have responded well. Traumatic and other soft-tissue lesions showing inflammatory and fibrotic change, such as bursitis, capsulitis, tenosynovitis, and tendonitis, are listed and seem logically suitable for treatment. Arthritic conditions, including osteoarthritis, osteochondritis, and especially early ankylosing spondylitis, respond by relief of pain and greatly increased mobility, and can be followed with exercises to maintain and increase joint range. True neuritis and neuralgia, as in post-herpetic pain, may be indications for trial of therapy.

Certain criticisms may be levelled at the work done.[3] Selection of cases on the basis of the known biological effects of ultrasonic energy, careful diagnosis, and objective clinical assessment of results have seldom been carried out. Subjective impressions and the psychological effect of a "new treatment" have been accepted too readily. Results have not been controlled by comparison with groups of cases treated by other well-tried methods already in general use. Thus the results reported in conditions such as fibrositis, lumbago, sciatica, and brachial neuritis are uniformly good, but, in view of the loose application of such diagnostic labels and the complete lack of any diagnostic criteria in the cases treated, the claims may well be compared to advertisements for proprietary brands of aspirin. They should be regarded with critical suspicion.

Potential dangers in treatment should be stressed in this largely unknown field, and only those well versed in physical therapy should undertake its use. Many of the tissues and pathological conditions which have been reported as dangerous to treat by this method are probably only so if high intensities are used. Despite the indiscriminate use of ultrasonics on the Continent, few serious mishaps have been reported. The treatment of malignant tumours is rightly condemned. Nevertheless the destructive effects of high energy ultrasonics might well be investigated further.[4] The use of ultrasonics after the manner of the diathermy cautery and by cross-fire methods in the production of deep effects without injury to superficial tissues may prove useful lines for investigation. The central nervous system, the eye, the ovaries and testes, the heart, the gravid uterus, growing zones of bones in children, and areas of cutaneous sensory loss are generally to be avoided because of the risks involved. Acute infective conditions should be treated with caution in view of the dangers of spread. It is likely that ultrasonics has a small but definite place in departments of physical medicine as a therapeutic agent. Careful and logical selection of cases on the known biological effects of ultrasonics should limit the application of treatment to the few conditions in which it is probably equal to, or better than, existing methods.

Work is progressing on the diagnostic use of ultrasonics, but results are so far too few to assess. The "optical" properties of ultrasonic waves are used. Reflected waves from objects or structures of definite outline and greater density than that of the surrounding tissues can be picked up and electronically translated into an image on the cathode-ray screen.[5] Examples are gallstones and foreign bodies not opaque to *x* rays. Tumour location will probably prove disappointing. At the Massachusetts Institute of Technology[6] a scanning ultrasonic beam is being used to outline the ventricles of the brain and will, it is hoped, prove useful in the diagnosis and location of intracranial lesions.

FESTIVAL SCIENTIFIC MEETING

In this Festival year the idea occurred independently to two professional organizations—the Royal Society of Medicine and the British Medical Association—to arrange a programme in which the advances of medicine could be assessed in a series of symposia. At the last meeting of the Council, Dr. T. Rowland Hill urged that the B.M.A. should plan some such celebration, especially in view of the fact that there would be no scientific part to the Annual Meeting of the B.M.A. this year. The Council warmly supported the idea, and as soon as it was looked into it was learnt that the Royal Society of Medicine had in fact gone far in making arrangements for a number of symposia in the various special branches of medicine. Almost immediately a proposal was made that those two organizations should combine in a joint sponsorship of a series of symposia, preliminary details of which will be found at page 166 of the *Supplement*. Although by the time the B.M.A. suggestion was mooted the Royal Society of Medicine had practically completed the details of its programme, it generously agreed to merge its interests with those of the B.M.A. in this Festival scientific meeting.

On the B.M.A. side seven symposia have been arranged and fitted into the joint programme. All the meetings will be held in the House of the Royal Society of Medicine, and any member of the B.M.A. will be able to attend these meetings, whether or not he is a Fellow of the Royal Society of Medicine. The only limiting factor is accommodation, which will have to be controlled by the issue of tickets, for which application will have to be made. Full details of the symposia will be given in a subsequent issue of the *Journal*. A happy outcome of this joint sponsorship was a proposal to hold in the middle of the meetings a Festival

Lecture, to be given in the Great Hall of B.M.A. House, and the two organizations have been fortunate enough to persuade Sir Henry Dale, O.M., to give this lecture.

MORE ABOUT PINK DISEASE

The latest publications from Australia on the subject of pink disease add to the confusion and difficulties to which we referred when commenting on a lecture[1] by Sir Stanton Hicks recently published in this *Journal*. We then expressed doubt about the theory that some form of adrenal insufficiency was concerned in the aetiology of pink disease, and mentioned that workers in Great Britain had failed to confirm the lowered sodium content of the blood plasma. Now a team of investigators in Melbourne headed by Dr. Howard Williams[2] have also reported negative results after an inquiry into this aspect of the hypothesis put forward by Cheek and Hicks. They studied the electrolyte pattern of 22 untreated patients suffering from pink disease and compared it with that of 22 normal healthy infants. Sodium estimations were made by the gravimetric method, whereas in Cheek's original investigations the emission spectrophotometer was used. But since Cheek and Hicks claim a *severe* electrolyte and water disturbance, the difference in methods alone can scarcely account for the fact which the Melbourne workers found on statistical analysis of their results "that there is no significant difference in the serum sodium levels of the two groups." A number of the determinations were carried out immediately after the patient's admission to hospital and again at the end of a week's observation. No significant difference was noted in the two series of observations. On the other hand, the authors found that the haematocrit, haemoglobin, and protein values were higher in infants with pink disease than in normal children and the chloride content of the blood significantly lowered. The nature of these changes is not understood.

Howard Williams and his colleagues then tested the value of salt and desoxycorticosterone in the treatment of ten selected and most carefully observed infants with pink disease. They failed to find "any really significant difference in the recovery rate" of five of these compared with five who did not receive this treatment. A point is made that rapid relief of symptoms in pink disease often occurs immediately after admission to hospital, and all their patients were carefully observed for one to two weeks before being selected for the treatment or control series. Elaborate precautions were taken to ensure that nurses and others were kept as ignorant as possible about the placing of the infants in the treatment or control groups. Another piece of evidence, also from Melbourne, is likewise negative. Bornstein and Trewhella[3] studied the urinary excretion of the breakdown products of adrenal steroids by measuring the 11-oxysteroids in infants with pink disease and in normal infants. No significant difference was found, and it is argued that this fails to support Cheek's suggestion of adrenal failure in pink disease. Alongside these two reports from Melbourne is another from Cheek.[4] Here he deals with what he terms the "later manifestations" of pink disease in older children, admitting that they have none of "the bizarre symptoms of classical infantile pink disease," and once again getting on to the doubtful ground of yet another hypothesis for "the nervous child." Attempts were made to estimate the adrenaline level in the blood of children with pink disease by biochemical methods, but compared with normal children no significant difference was noted by the method used. Cheek takes his hypothesis a stage further on this occasion with suggestions of a disturbance of porphyrin metabolism, but it would now seem to be more important to clear up the discrepancies between the Adelaide and Melbourne results of serum sodium measurements in pink disease.

1 *British Medical Journal*, 1951, **1**, 317. See leading article on p. 343.
2 *Med. J. Aust.*, 1951, **1**, 363.
3 Ibid., 1951, **1**, 385.
4 Ibid., 1951, **1**, 353.

INCLUSION BODIES

It has been customary to designate as "inclusion bodies" any atypical structures seen in cells believed to be infected with a virus. Consequently the inclusion bodies are a miscellaneous assortment of intracellular formations of varying nature and significance. Some, such as the Negri bodies of rabies and the Bollinger bodies of fowl-pox, are sufficiently characteristic to be of diagnostic value. Others do not differ in any essential respect from structures occasionally seen in cells when no virus is present. As Ludford[1] has pointed out, "there has been an unfortunate tendency to study infected cells cytologically, without a preliminary study of the morphological changes which occur in the same cells during autolysis, in the absence of micro-organisms."

The commonest form of intranuclear inclusion is a rounded body, larger than the nucleolus, which stains intensely with acid dyes such as eosin, and sometimes occupies almost the entire nucleus. Such bodies have been variously interpreted as accumulations of virus particles embedded in a matrix, or as the result of the reaction of the cell to the presence of a virus. They have been reported in kidney cells of many mammals and birds by Cowdry, Lucas, and Fox,[2] who could find no justification for associating them with a virus infection. Similar bodies were also produced with chemicals by Olitsky and Harford.[3] Without confirmatory evidence, then, it is unjustifiable to accept the presence of acidophil intranuclear inclusions alone as proof of virus action.

Some at least of the cytoplasmic inclusion bodies may well be masses of virus particles (elementary bodies) embedded in, or surrounded by, products of cellular reaction. This applies particularly to the inclusion bodies occurring in fowl-pox, molluscum contagiosum, vaccinia, and psittacosis, in which it is possible by dark-ground illumination to demonstrate that the mature

1 *Cytology and Cell Physiology*, p. 373, edited by Bourne, G. H., 1951, Oxford.
2 *Amer. J. Path.*, 1935, **11**, 237.
3 Ibid., 1937, **13**, 729.
4 Ibid., 1929, **5**, 1.
5 *Cancer Res.*, 1943, **3**, 585.
6 Ibid., 1947, **7**, 421.

inclusion bodies are composed of minute particles. Woodruff and Goodpasture[4] provided unequivocal evidence that the Bollinger bodies of fowl-pox contained the virus by isolating single bodies with a micromanipulator, washing them in saline, and then inoculating them into the skin of a chick. A single body could produce the typical warty lesion of fowl-pox, but the saline in which it had been suspended before inoculation was innocuous.

In a study of inclusion bodies in warts published elsewhere in this issue Drs. A. Lyell and J. A. R. Miles have reported both intranuclear and cytoplasmic eosinophil inclusions in what they term type I warts and which they suggest should be renamed "myrmecia." They were unable by tryptic digestion to free the inclusion bodies from the epidermal cells, as can be done with the Bollinger bodies of fowl-pox. Neither could they demonstrate free elementary bodies in the digest, by either dark-ground illumination or electron microscopy. They have wisely avoided any discussion whether these inclusions are masses of virus particles or reaction products of the cells to virus infection; but it is relevant to note that, in cells of the Rous fowl sarcoma No. 1, Tenenbaum and Doljanski[5] observed with the ordinary light microscope both intranuclear and cytoplasmic eosinophil inclusion bodies, while by electron microscopy Claude, Porter, and Pickles[6] have photographed minute granules, both isolated and in chains, far too small to be visible with the light microscope, but of approximately the same size as that determined for the Rous sarcoma virus by other methods.

THE CAUSE OF WARTS

In the records of folk-medicine warts are accepted as being infective.[1 2] Clinical histories suggest they are contagious and auto-inoculable. They conform to certain of the disease patterns produced by viruses, since they are predominantly a disease of childhood, and further are a "conditioned" infection, in which mere contact of virus and host seems insufficient to produce obvious disease, in this resembling poliomyelitis and the common cold. Local resistance and susceptibility are so delicately adjusted that other factors are needed to tip the balance, and there is much evidence that psychological influences can be responsible, as well as local disturbances like trauma or excessive sweating.

Jadassohn demonstrated infectivity by a successful series of inoculations with wart tissue. Cuiffo, Wile, and Kingery and others showed that the infective agent passed through a Berkefeld filter and was presumably a virus.[3] Intradermal inoculation experiments by other investigators suggested that all clinical varieties of infective warts were caused by the same agent,[4] and it had been supposed that their different features depended on the nature of the affected site. Lipschutz[5] described nuclear inclusions in young warts, but until recently the evidence had not advanced beyond this stage. These warts appear to infect only man, and animal inoculation is unsuccessful. Felsher[6] failed to grow material from warts on the chorio-allantoic membrane of the chick embryo. Brain[7] recorded that no circulating antibodies could be demonstrated.

In 1950 Strauss, Bunting, and Melnick[8] confirmed that some warts contained inclusion bodies and reported that they were able to demonstrate, by electron microscopy, elementary bodies or virus-like particles crystalline in structure and averaging 52 mμ in size. They suggested that the lesions containing inclusions were distinctive papillomata clinically distinguishable from warts. Blank, Buerk, and Weidman[9] reported the finding of intranuclear inclusions in warts in 34 of 65 lesions examined. As these inclusions were irregularly distributed among the tumour cells, they suggested that failure to examine serial sections might have been responsible for their findings. They did not make a clinical differentiation between types as did Strauss. Lyell and Miles elsewhere in this issue state that inclusions can be demonstrated in plantar, palmar, and periungual warts but not in the more superficial horny excrescences on hands, scalp, and knees. Their claim that the two varieties do not occur together in the same subject will not, however, be accepted by other observers. It may be that, as viruses are subject to variability (probably corresponding to mutation), such variation may affect their affinity for particular tissues, the virulence of their attack, and their resistance to external influences. This may alter the morphological picture produced. The report of Lyell and Miles opens up intriguing possibilities of studies along these lines and should help to establish more fully the cause of these tumours.

Until the aetiology is more clearly understood, treatment of these trivial but troublesome lesions remains unsatisfactory. With a condition which is self-limiting and so susceptible to secondary influences assessment of therapy is difficult. With fuller knowledge it may be possible to explain the success of psychotherapy. Chemotherapy is of no value, and podophyllin, which is successful in treating condylomata acuminata, is not effective in more keratinized warts. Removal or destruction of the lesions by curettage, diathermy, or freezing remains the most reliable treatment.

1 Bett, W. R., *Practitioner*, 1951, **166**, 77.
2 Zwick, K. G., *Arch. Derm. Syph., Chicago*, 1932, **25**, 508.
3 *J. Amer. med. Ass.*, 1919, **73**, 970.
4 Frey, E., Serra, A., and Ullman, E. B., quoted by Goodman, J., and Greenwood, A. M., *Arch. Derm. Syph., Chicago*, 1934, **30**, 659.
5 *Arch. Derm Syph., Wien*, 1924, **148**, 201.
6 *J. Invest Derm.*, 1947, **8**, 123.
7 *British Medical Journal*, 1936, **1**, 934.
8 *J. Invest. Derm.*, 1950, **15**, 433.
9 Ibid., 1951, **16**, 19.

A POLIO-LIKE EPIDEMIC IN ICELAND

Virus diseases occupy a larger amount of space every year in the annual report[1] of the International Health Division of the Rockefeller Foundation. In the recently published report for the year 1949 "virology" is described as a young and rapidly expanding science, with still much to be learned of the fundamental nature, classification, and range of parasitism of viruses in general, and with new viruses constantly coming to light. Gradually scientific workers are succeeding in linking some of these viruses to diseases of hitherto unknown aetiology; a number of them are suspected of having a wide geographical distribution.

One interesting observation in the report relates to an unusual epidemic in Iceland, having some features in common with poliomyelitis. Until about 1945 poliomyelitis, which had been recognized in Iceland for nearly 50 years, had followed more or less the usual pattern in epidemiology, age incidence, and seasonal distribution. But in that year the age incidence began to shift upward, and in the following year the seasonal incidence changed so that the peak, instead of being in the late summer and early autumn, was in the late autumn and early winter. Both 1945 and 1946 were epidemic years, which itself was unusual, since epidemic years had not tended to occur in succession. In the late autumn of 1948 another epidemic wave appeared and extended through the early months of 1949. During this period more than 1,100 cases were reported (this in a population of only about 120,000), and in some districts the morbidity rate reached 7%. Youths and adults were attacked more frequently than young children, and the highest incidence was in the late autumn and winter. It was arranged that a member of the staff of the International Health Division should visit Iceland in the autumn of 1949, partly in response to an invitation from the Icelandic Government for assistance in establishing a laboratory for the diagnosis of human viral diseases at Reykjavik, but also to study the epidemic should it recur. As it turned out, in October, 1949, there were no active cases of the disease available for observation, and the visitor had to fall back upon the study of statistical records and case histories and interviews with district health officers and other medical men who had followed the course of the epidemic. This information, however, all went to show that the epidemic was of an unusual nature, differing in clinical manifestations and epidemiological behaviour from true poliomyelitis.

Sigurdsson and his colleagues[2] have described the features of this epidemic in some detail. The disease was characterized by severe pain in the back and in the nape of the neck, with some fever. Paraesthesia and hyperaesthesia were common, and approximately 28% of the patients developed muscular paresis, usually slight but sometimes severe. The fever lasted for weeks in some cases, and relapses were noticed in which fever, sensory changes, and paresis all recurred. The slightest physical exertion or exposure to cold aggravated the symptoms and brought on new manifestations of the disease. Recovery from slight paresis was good, but some patients with more severe symptoms have remained seriously disabled. Polyarthritis developed after the illness in a number of cases. In the cerebrospinal fluid protein and cells were increased. No deaths occurred during the epidemic, and therefore the pathological changes are unknown. There was no evidence that the infection was conveyed by water, milk, or other food, and personal contact appeared to be the most probable means of transmission. It has been suggested that the virus concerned may be one of the Coxsackie group, but if so its manifestation in Iceland, either as a result of a more virulent strain or greater host susceptibility, is more serious than illness associated with this group of viruses in the United States and elsewhere. It seems possible that the causal agent was either an abnormal poliomyelitis virus of low virulence or a new neurotropic virus. If the disease recurs a Rockefeller commission will probably be sent to Iceland to obtain more precise information about its aetiology.

[1] The Annual Report for 1949 of the International Health Division of the Rockefeller Foundation, 1950, New York.
[2] *Amer. J. Hyg.*, 1950, **52**, 222.

KIDNEY LESIONS IN DIABETICS

Control of the blood sugar by diet alone or diet plus insulin is now the rule in the management of diabetes mellitus; and almost all careful and co-operative diabetic patients have a good expectation of life and are free from the hazard of acidosis coma. But prolonged insulin-controlled diabetes is not without other hazards—those of cardiovascular and renal complications. In 1898–1914 64% of diabetic deaths were due to coma, and the average length of survival with diabetes was 4.9 years, whereas in 1944–6 67% of diabetic deaths were due to cardiovascular and renal complications, and the average length of survival was 14.1 years.[1] Clearly these complications still present a formidable challenge in the management of diabetes mellitus. When fully developed they can be recognized by quite characteristic signs, if the importance of searching for them in the diabetic patient is not forgotten. Little is known of their cause or treatment. One of the renal complications, intercapillary glomerulosclerosis (the Kimmelstiel–Wilson lesion), deserves special notice, because it is evidently peculiar to diabetes mellitus. There is still some confusion over its pathological features and no agreed clinical hallmark of its presence. The confusion has arisen because intercapillary glomerular hyalinization may be found either as a nodular or as a fine diffuse form.[2,3] The latter is probably more common among diabetics but is not distinctive clinically. It is the nodular lesion that was described originally by Kimmelstiel and Wilson[4]; they found it in a proportion of nephritic kidneys, and reference to the histories of the patients indicated a common clinical syndrome of diabetes mellitus, albuminuria, oedema, and hypertension. In the main this clinical syndrome has been confirmed,[3,5-7] apart from some confusion arising from attempted correlation with other than the nodular glomerular lesions.[8,9] Elsewhere in this issue Dr. I. Gilliland puts forward further good evidence to support the existence of this syndrome. Out of 10 patients found at necropsy to have Kimmelstiel–Wilson lesions in their kidneys eight had presented during life all the features of this syndrome, which were never found together in any one patient in the whole series without the kidney lesion also being present. Besides hypertension, oedema (often mild), and moderate albuminuria, these patients suffered also from two other diabetic

1 Joslin, E. P. *Treatment of Diabetes Mellitus*, 1946, London.
2 Kimmelstiel P., and Porter, W. B., *New Engl. J. Med.*, 1948, **238**, 876, 908.
3 Bell, E. T., *Renal Disease*, 1950, London.
4 *Amer. J. Path.*, 1936, **12**, 83.
5 Anson, L. J., *Sth. med. J.*, 1938, **31**, 1272.
6 Newburger, R. A. and Peters, J. P., *Arch. Intern. Med.*, 1939, **64**, 1252.
7 Laipply, T. C., Eitzen, O., and Dutra, F. R. ibid 1944, **74**, 354.
8 Siegal, S., and Allen, A. C., *Amer. J. med. Sci.*, 1941, **201**, 516.
9 Horn, R. C., and Smetana, H., *Amer. J. Path.*, 1942, **18**, 93
10 Ashton, N., *Brit. J. Ophthal.*, 1949, **33**, 407.
11 Friedenwald, J. S., *Trans. Amer. Acad. Ophthal.*, 1948, **53**, 73.
12 Rundles, R. W., *Medicine*, 1945, **24**, 111.

complications—neuritis and retinitis. Because the underlying vascular abnormality is probably similar,[10-12] the presence of neuritic and retinal complications should always lead to a search for other features of the nephrotic syndrome.

THE ELDERLY IN NO-MAN'S-LAND

In the House of Lords debate on the care of the aged last week (see page 956) one speaker deplored the fact that some people refused to accept the responsibility of looking after their parents. Fortunately most old people remain physically and mentally fit, and their families are well able, and usually willing, to care for them. The minority who need outside assistance fall into two groups—those who are old and infirm but not really sick, and those who are old and physically or mentally sick. Among the agencies providing help are the National Assistance Board, the local welfare authorities, the regional hospital boards, and many voluntary organizations. The largest gap in the services for the aged is the no-man's-land between local authorities and regional hospital boards. In general it is the job of local authorities to see that the elderly receive the domestic and nursing help they need in their own homes—the National Assistance Board providing the financial assistance. For those who, though not ill, can no longer live on their own and have no relatives to care for them, the local authority is supposed to find accommodation in welfare homes or hostels. Since the end of the war 300 of these homes have been opened in England and Wales, but a great many more are needed before the urgent demand for vacancies can be met. Local authorities which have taken the trouble to organize really effective domiciliary services for the aged —such as nursing, mobile physiotherapy, home-helps, and "meals on wheels"—have been rewarded by a reduction in the number of old people wishing to enter hostels.

The part of the regional hospital boards is to provide hospital treatment for the old, as, indeed, for any other group of the population, though whether all hospitals are giving elderly patients a fair deal in the apportionment of beds is another matter. But the main trouble begins when the elderly patient is due for discharge: many need special attention and encouragement before returning to relatively normal life, and for others medical supervision and more or less permanent nursing care will be required for the rest of their lives. It is for the latter type of patient that "long-stay annexes" are intended, but here again it will be many years before enough places can be provided. In the meantime the blocking of hospital beds seems unavoidable. Lord Kershaw, speaking for the Government in the House of Lords debate, admitted that the problem of hospital beds "nearly defied solution." A step towards its solution, however, has been taken by the King Edward's Hospital Fund and the National Corporation for the Care of Old People, which have sponsored the establishment in some areas of what are called "half-way houses."[1] It is not intended that elderly patients will remain in these houses for very long, and they can be admitted from either side of no-man's-land. From the hospital they can pass through the half-way house as a process of rehabilitation before returning home or to the welfare hostel, and from home or hostel they can be admitted to the half-way house for investigation and perhaps for a period of recuperation. These half-way houses, which have many features in common with nursing-homes, are on the hospital side of the gap. On the welfare side there have been efforts to provide "sheltered" accommodation in hostels where the aged can be properly looked after when they do have to take to their beds. Financial and staffing difficulties have been keeping both these projects in the experimental stage, but a glance at the histogram on page 959 shows how necessary it is to provide more homes for the elderly now, for the demand is likely to increase.

1 *The Times*, April 10, 1951.

SIR CHARLES HASTINGS MEMORIAL FESTIVAL

The memory of Sir Charles Hastings, founder of the Provincial Medical and Surgical Association 119 years ago, will be honoured at a festival to be held on May 30 at Worcester, the town where he did his life's work. A man of great industry and ability, as well as a prolific writer on medicine and natural history, Hastings soon made his mark at Worcester. As a correspondent describes on another page, he was elected at the age of 24 to the post of physician to the Worcester Infirmary and held it for 44 years, resigning in 1862. For most of that time he was the leading physician in Worcestershire and the surrounding counties.

In 1832 Hastings called a meeting at the Worcester Infirmary, and it was then that a decision was taken to found the Provincial Medical and Surgical Association, the forerunner of the B.M.A. He was himself for 11 years the secretary of the association and its leading spirit. Because of increasing duties he had to resign that post in 1843, when he was appointed permanent president of the council and treasurer. For his distinguished services to the profession he was knighted in 1850, and when the G.M.C. was formed under the Medical Act of 1858 Hastings was appointed to that body as a Crown nominee, an appointment he held until 1863. He died three years later, at the age of 72.

At the festival on May 30[1] a memorial service will be conducted in the cathedral by the Bishop of Worcester. Dr. W. H. McMenemey will deliver the first Sir Charles Hastings Memorial Lecture, and an exhibition of relics of Sir Charles Hastings will be on view in the board-room of the Worcester Royal Infirmary. Lunch (1 guinea) and tea will be provided for visitors, who should apply for tickets to Dr. M. P. Martin, 109, Laugherne Road, Worcester. Hospitality is also offered by the members of the Worcester and Bromsgrove Division to visitors wishing to stay the Tuesday or Wednesday night in Worcester, and they should write to Dr. C. Mackie, The Lower House, Stourport. Visitors are assured of a warm welcome at these celebrations.

1 *British Medical Journal Supplement*, 1951, 1, 151.

REFRESHER COURSE FOR GENERAL PRACTITIONERS

CORONARY ARTERY DISEASE—II. TREATMENT

BY

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As the causes of coronary sclerosis remain undetermined, a direct therapeutic approach is at present denied to us. There is as yet no conclusive evidence that such remedies as iodides, thyroid, sex hormones, choline, or vitamin E, which have been used in the experimentally induced arteriosclerosis of animals, retard or reverse the arteriosclerotic process in the human coronary tree. Nevertheless, when treatment is directed to the leading clinical manifestation much good can be done.

Although the three syndromes—angina pectoris, coronary insufficiency, and coronary thrombosis with infarction—overlap and may on occasion be difficult to distinguish, yet the methods employed in their treatment can be sharply defined. In each instance the objects should be to avoid the precipitating cause of the attack, to promote healing if myocardial damage has been sustained, and to prevent incapacitating and commonly fatal complications.

Angina Pectoris

Many factors contribute to attacks of effort pain. Attention should first be directed to body weight. The practitioner can obtain useful help from height and weight tables if he will weigh his patient and take note of the deviation from the theoretical standard for sex, age, and height. If obesity be reduced at a rate of 1 to 2 lb. (0.45 to 0.9 kg.) each week by the use of a low-calorie diet, a corresponding freedom in bodily activity is commonly observed and greatly appreciated by the patient. The aim should be to maintain weight within 10% of normality.

Even a minor degree of anaemia can contribute to the ease with which attacks of pain are induced. Haemoglobin determinations take only a minute or two. Treatment with iron or liver, according to the type of anaemia present, can be of immense benefit to the anginal patient.

There are other contributory factors. Foci of infection about the teeth or elsewhere should be corrected, tobacco should be interdicted for a month or two as a therapeutic trial, and efforts should be made by medical means to relieve dyspepsia whether it be peptic, biliary, or nervous in origin.

Exercise should be encouraged up to the limit of tolerance and needless restrictions should be avoided. In effect this usually means some reorganization of the way of life, but most patients soon discover their limitations and act accordingly. It is a good rule to recommend a short rest (thirty minutes or more) after each meal, an extra hour in bed each night, and half a day or more in bed each week. It is necessary to advise two to three weeks in bed only when anginal attacks are severe, exhausting, or increasing in frequency, or when an actual coronary thrombosis appears imminent.

It is important to instil a measure of confidence. Rest and reassurance are of value from this point of view, and in patients of nervous temperament and emotionally sensitive the gentle sedation derived from small doses of barbiturates has a definite place in treatment. Phenobarbitone can be given by mouth in doses of ½ gr. (32 mg.) or more in tablet form twice or thrice daily. It is necessary to correct insomnia and relieve anxiety.

Glyceryl trinitrate in tablet form (1/400 to 1/50 gr.—0.16 to 1.3 mg.) is the drug of choice. Until its effects have been determined a small dose should be used. It must be allowed to dissolve in the mouth. When used in this way the action of the drug is at its height in two to three minutes and passes off within half an hour or so. It can therefore be used both for the relief of pain and for its prevention. Tablets of nitroglycerin, taken in anticipation of discomfort, do much to make life more tolerable for many sufferers from angina. When attacks are more frequent and difficult to anticipate a tablet can be sucked at regular intervals of an hour or two during the day; additional tablets can be taken should the necessity arise. The patient should be encouraged to use them freely with the object of preventing attacks.

Other drugs are seldom necessary and seldom as effective. Papaverine, in virtue of its prolonged antispasmodic action, is sometimes useful in the prevention of nocturnal attacks when taken by mouth at bedtime in tablets or powders containing 1½ to 3 gr. (0.1 to 0.2 g.). Although commonly prescribed, there is little convincing evidence to justify the continued oral use of xanthine drugs such as theophylline in its various combinations in the day-to-day treatment of coronary sclerosis. Recently khellin, an extract of the seeds of an Eastern Mediterranean plant, has been shown experimentally to have coronary dilator properties. It has been given intramuscularly in doses of 50 to 100 mg. daily, and by mouth in tablets of 40 mg. or more thrice daily, but in anginal patients the reports on its use are conflicting.

Coronary Insufficiency

Coronary insufficiency depends for its effective treatment upon the correction of the precipitating cause. Undue physical or mental strain, intense enough to produce severe anginal symptoms, with the possibility of irreversible change in the deeper subendocardial layers, implies at least a week to ten days' rest in bed. Nitrites and sedatives may be used freely in these attacks, and opiates if necessary. Under other conditions different remedies will prove desirable. A paroxysm of tachycardia productive of anginal symptoms will require, in addition to rest and sedatives, digitalis or quinidine sulphate according to its nature. Normal rhythm may thus be restored and precordial

distress relieved. A hypertensive crisis may call for a free venesection, whereas a blood transfusion will prove necessary for the prompt relief of the myocardial ischaemia of post-operative shock or a massive haemorrhage.

For recurrent and severe anginal attacks at rest, when no precise exciting cause can be determined and when the response to full and repeated nitrite dosage is only partial and transient, resort may be made to division of the pain-conducting pathways either by the technique of paravertebral alcohol injection or by cervical sympathectomy on one or both sides. Neither procedure has yielded encouraging results in my experience.

Bold attempts to revascularize the impoverished heart muscle have also been practised. Grafts of intercostal muscle, lung, or omentum, supposedly carrying a fresh blood supply to the inadequate coronary circulation, have been used without much benefit. These procedures are largely experimental and the beneficial clinical results so far claimed lack conviction.

Conservative Treatment of Coronary Thrombosis

An attack of coronary thrombosis usually responds well to treatment aimed at the relief of pain, correction of shock, promotion of healing, and prevention of further thrombotic or embolic episodes and their complications.

For the excruciating pain, the restlessness, the paroxysmal dyspnoea, or the attack of acute pulmonary oedema there is no better drug than morphine (¼ gr.—16 mg.) which may be repeated in half an hour if symptoms are not abating. In the most urgent cases 1/6 gr. (11 mg.) of morphine diluted in 5 to 10 ml. of sterile water may be *slowly* injected intravenously. In doing so the injection should be stopped before completion if obvious relief is obtained or if the respirations are unnaturally slowed.

Shock may be countered by reassurance, warmth, and relief from pain and restlessness. Transfusion of 150 to 250 ml. of blood, plasma, or normal saline is sometimes justifiable if given very slowly to the worst cases, but there is always the danger of overloading the heart and inducing pulmonary oedema, itself a contraindication to an increase in blood volume. Nikethamide and leptazol (each 1 ml.) are commonly used intramuscularly. Their main influence appears to be the counteraction of respiratory depression.

There is sound justification for the use of oxygen, but to be effective in the relief of cyanosis, pain, and restlessness it must be delivered in high concentration (50 to 75%) at 6 to 10 litres a minute by B.L.B. mask or tent. Nasal catheters smeared with a local analgesic ointment are useful substitutes if comfortably tolerated. Oxygen therapy should be continued as long as the ashen-grey hue in the skin and nail-beds persists.

Rest in bed must usually be maintained for six weeks or thereabouts, and the more complete the inactivity during the first three or four days the better. During this time the patient should do nothing for himself. He is to be fed and washed; visitors must be excluded, and sleep ensured. Constipation can be encouraged for the first few days and the diet restricted to fluids and soft foods. When the acute symptoms have subsided increasing liberties may be granted. Patients can then begin to move about in bed, practise leg exercises, feed themselves, and be permitted the use of a bedside commode in preference to all the inconvenience and discomfort of the bed-pan. In the presence of cardiac asthma or acute pulmonary oedema permission to leave bed and sit upright in a chair is a concession which has a physiological basis. The change of posture eases the respiratory and circulatory burdens, lessens fatigue, and makes for greater comfort. By the end of four weeks, massage and active movements should be in daily use preparatory to the patient getting up and moving about quietly in his room.

During the entire illness great care should be taken of the bowels. While constipation is usual and of advantage during the acute phase of the illness, thereafter the daily evacuation of a soft easy motion may be aided by an emulsion of liquid paraffin and agar (2 to 4 dr.—7 to 14 ml.) or small repeated doses of milk of magnesia (1 to 4 dr.). The addition of suitable quantities of fresh and dried fruit to the diet should be encouraged. Brisk purgatives and bulky enemata are exhausting and therefore better avoided.

It is not considered good practice to prescribe digitalis in the early weeks after an acute infarction. It is said to enhance the clotting tendency and to favour the development of abnormal rhythms, ventricular tachycardia in particular. On the other hand, its use is justified in the presence of congestive failure of sufficient degree to produce respiratory distress, particularly when the patient's state is obviously deteriorating. It is better given in moderate amount—1 to 2 gr. (65 to 130 mg.) of powdered digitalis thrice daily—rather than in massive doses. In these circumstances my preference is to select digoxin (0.25 mg. by mouth thrice daily), supplemented by mersalyl intramuscularly in doses of 1 ml. on alternate days—a combination very effective in clearing the lungs of oedema and congestion. Quinidine should be used only with electrocardiographic control for the arrhythmias.

Among hospital patients, treated as we believe under the best available conditions, conservative measures yield a mortality rate of 33% in this country.

Anticoagulants in Coronary Thrombosis

Heparin and "tromexan," begun early in the illness, are believed to owe their effectiveness to their ability to restrict the spread of the thrombus and thus limit the size of the infarct and prevent its extension. They reduce the tendency to deposition of thrombi within the ventricles and peripheral veins. Pulmonary and other infarcts are thus seldom encountered when anticoagulants are used efficiently. It may well be that these drugs have other actions of benefit to the patient stricken with an acute infarct. Increasing experience confirms their undoubted value and marks the use of these drugs as an outstanding advance in therapy.

Both are started simultaneously, heparin by injection and tromexan by mouth. The former, if given intravenously at six- to eight-hour intervals in doses of 10,000 units, will prolong the clotting time to 20 minutes, three or four times the normal value, an hour after the injection. It is usually necessary to continue heparin for only 24 to 36 hours, by which time the tromexan has generally produced a sufficient reduction of the prothrombin content of the blood.

Two doses of tromexan are given daily, usually at 12 noon and 8 p.m., a total of four 300-mg. tablets being taken by mouth on the first day of treatment.

Thereafter daily laboratory control is essential, the quantity of tromexan prescribed being adjusted from day to day with the object of maintaining the patient's prothrombin clotting time at a level two to two and a half times the control prothrombin time. There is unfortunately no clinical guide to tromexan dosage. The normal prothrombin time lies between 17 and 19 seconds, varying considerably with the technique employed. The effective therapeutic level therefore ranges between 34 and 48 seconds.

When tromexan yields a prothrombin time of 35 seconds or more, the injections of heparin are stopped. The tromexan is continued for four weeks from the onset, or for three weeks from any thrombo-embolic complication, whichever is the longer. The daily dose is regulated according to the laboratory report on the 9 a.m. prothrombin time for that day.

The response to the drug varies greatly from patient to patient and from day to day in the same individual, but, if the dose is regulated according to the standards advocated, difficulties are seldom encountered and serious bleeding is rarely observed.

Tromexan is a much safer drug than dicoumarol. Its dose is larger and more easily regulated, and on its discontinuation the prothrombin time returns to normal in 24 hours—an advantage should haemorrhage occur.

The haphazard use of these drugs without competent laboratory control cannot be too strongly condemned. The practitioner can always begin treatment with heparin in the patient's own home, but at present tromexan, which has replaced dicoumarol, cannot be used without daily estimations of prothrombin time, which is a laboratory procedure demanding the co-operation of competent technicians. Furthermore, continuous supervision, such as only the hospital can provide, safeguards the patient against the risk of serious haemorrhage by constant observation and ready availability of the blood bank.

Bleeding may be sudden and profuse. A transfusion may be required at short notice. Blood which has been stored for more than 24 hours is said to be less effective than fresh blood in the correction of the hypoprothrombinaemia. As the beneficial effect of a blood transfusion on the bleeding tendency may last only for two to six hours, repeated transfusion over a period of several days may be necessary. A prothrombin clotting time in excess of 75 seconds is usually regarded as a danger signal and an indication for vitamin K (intravenously), a dose of which may be repeated four-hourly until the prothrombin time is reduced to well within the therapeutic range.

It should be emphasized that anticoagulants are contraindicated, or at best used with great caution, in the presence of hepatic or renal disease, during pregnancy, or shortly after major operations. Severe anaemias also countermand their use. Peptic ulcer occasionally coexists with serious coronary disease. As fatal bleeding may occur from a duodenal or gastric ulcer, when the prothrombin time is reduced by tromexan the patient should be questioned about recent dyspeptic symptoms before anticoagulants are employed.

Treated in this way patients stricken with acute myocardial infarction make remarkable progress. They look better and feel better in a shorter space of time than those denied this form of treatment. Complications are reduced, embolic phenomena are infrequent, convalescence advances more quickly (though advantage should not be taken of this to shorten the time in bed), and the mortality rate is reduced by more than half. It is therefore a method of treatment which should be made available for every sufferer from acute coronary thrombosis.

Other Syndromes

The arrhythmias of coronary origin are generally permanent, though auricular fibrillation in a paroxysmal form can recur frequently, prove difficult to prevent, and cause distress in virtue of the tachycardia. The continuous use of digitalis in regular courses of seven to ten consecutive days with three or four days' intermission between each often proves helpful, not so much in preventing attacks as in easing their distress by restraining the ventricular rate and thereby avoiding the embarrassment of the tachycardia. Complete heart-block is an irremediable condition, but recurrent Stokes–Adams seizures can be prevented by ephedrine, ½ gr. (32 mg.), by mouth thrice daily.

A major problem in therapeutics is the rational treatment of acute left ventricular failure as manifested by attacks of paroxysmal dyspnoea (cardiac asthma) or pulmonary oedema. When precipitated by coronary thrombosis, shock (or peripheral forward failure) is combined with congestive or backward failure. In these circumstances the energetic treatment of the one may aggravate the other form of failure. For instance, a venesection may well be justified in many cases of acute pulmonary oedema, but if aggravation of the shock-like state occurs, with a further fall in blood pressure and a lowering of haemoglobin, the heart may be weakened further and the patient's condition be worsened. It is necessary to steer a middle course, using cautiously approved methods of known value. Morphine, ¼ gr. (16 mg.), is of great benefit. Wheezing denotes bronchospasm and may be taken as an indication for aminophylline, 0.5 g., administered intravenously over a five-minute period or by rectum in the form of a suppository when the distress is milder. Oxygen is indicated. If these measures are not helpful within half an hour, then, despite the presence of a possible infarct, 1 mg. of digoxin may be given intravenously, diluted in 5 to 10 ml. of normal saline, as a life-saving measure. To help unload the pulmonary oedema intravenous digoxin injections can usefully be combined with 1 ml. of mersalyl. A venesection is justified only when shock is absent or mild.

The methods employed in the treatment of the more chronic forms of congestive failure occurring in the course of arteriosclerotic heart disease do not differ significantly from those in common use. Adequate rest, the correction of insomnia, a low-sodium diet, digitalis according to tolerance, and mercurials intramuscularly are the main items which require to be adapted to the individual's particular requirements.

Recent tests on over 11,000 unselected persons of varying ages from all walks of life, using the Ishihara pseudo-isochromatic plates, have shown a colour-blindness incidence of 4.97% for Chinese males and 0.71% for Chinese females (*British Journal of Ophthalmology*, 1950, **34**, 744). These figures are considerably lower than those previously produced from smaller scale investigations.

THE NUFFIELD ORTHOPAEDIC CENTRE, OXFORD

BY

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In order to further the progress of orthopaedic surgery and traumatology Lord Nuffield, in December, 1949, made a donation of £50,000. This donation is being used to organize a centre for the study, research, and treatment of orthopaedic and traumatic conditions, which in his honour has been named the Nuffield Orthopaedic Centre.

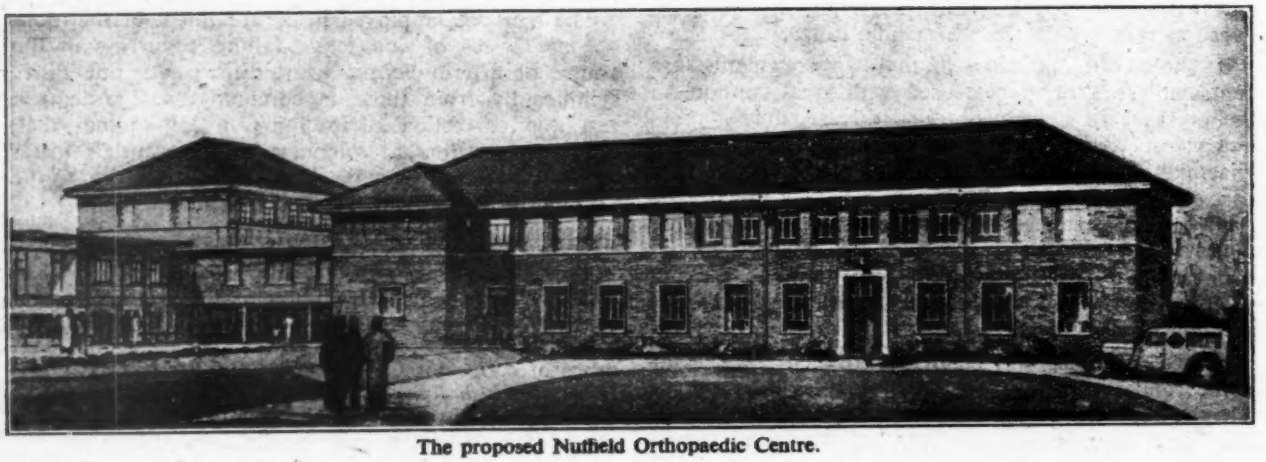
It is probable that the increasing collaboration between clinicians and research workers is one of the factors responsible for modern medical progress. It may be easy to find convincing examples of the benefits that this association brings to both types of workers and ultimately to medical progress in general, and, as the author has had the opportunity of stressing this point before,[1] it will not be elaborated further here. This assertion appears to be true for every branch of medicine, and it seems certain that the study of the pathology of the locomotor system will also benefit from this double-sided method of approach—that is, accurate clinical observation and scientific recording of experimental data obtained from research on laboratory animals.

It is common knowledge how orthopaedic surgery became detached from the main body of surgery by the outstanding contributions of a handful of men such as Hugh Owen Thomas, Louis Ollier, Robert Jones, and Vittorio Putti—to mention only a few of the past generations, who in not much more than fifty years created this specialty and brought the study of the diseases of the locomotor system from the elementary state in which they found it to the satisfactory conditions of the present day. H. O. Thomas in particular was responsible for spreading the conviction that crippling disabilities could be both cured and prevented in the great majority of cases. His work and that of his immediate follower, Sir Robert Jones, proved so successful that in the hands of people such as G. R. Girdlestone, so recently and sadly removed from us, the prevention and treatment of a great number of crippling diseases have reached a high pitch of perfection. It seems doubtful now whether much progress can still be achieved by the method of observation alone, as was practised by all these great orthopaedic surgeons.

Combined Clinical and Experimental Approach

I have had the privilege, on more than one occasion, of collaborating with research workers in the investigation of problems which had been detected in the clinical wards.[2 3 4] Having thus been engaged for a good number of years both in clinical work as an orthopaedic surgeon and also in experimental research on animals, I may be allowed to venture an opinion on the possibilities of a co-ordinated centre where the investigation of clinical problems can be approached from both the clinical and the experimental aspects. As an orthopaedic surgeon several examples spring to one's mind of subjects which are awaiting such a combined approach; osteomyelitis might be given as an example. Haematogenous osteomyelitis is due initially to a vascular thrombosis in the bone, but we know next to nothing about the rearrangement of the blood supply once the condition has become established. This gap in our knowledge should not surprise us, since as yet we know nothing of the blood supply of normal bone—an incredible situation when one recalls that bone is one of the most important sources of blood. Thus a well-planned and meticulous investigation of the blood supply of the bone in normal and pathological conditions is essential if we are to understand the intimate problems of bone pathology. But without correlating the results thus obtained with the findings in human pathology—in this case haematogenous osteomyelitis—the information gained may be incomplete or even erroneous. For this reason the clinical study and histories of cases in the wards of the centre must be accurate and as complete as possible.

Poliomyelitis is another condition in which such integration of clinical observations and experimental work is urgently needed. At present orthopaedists and neurologists collect data from clinical material somewhat independently, and virus experts investigate the characteristics of virus diseases in animals. But the role that muscle plays in the disease is still undetermined, notwithstanding that orthopaedic surgeons and physiotherapists have centred their interest on muscular recovery for many years. The wealth of experimental data now available on the damage to the central nervous system contrasts sharply with the scarcity of information on the phases through which the muscle passes in this



The proposed Nuffield Orthopaedic Centre.

paralysing disease; this knowledge might explain the very late, and not infrequently unexpected, recoveries in poliomyelitis. It is clear that without careful experimental research the study of both the changes in the blood supply of bone and of muscle recovery in poliomyelitis is unlikely to be fruitful, if not totally impossible.

Facilities Required for Orthopaedic Research

An organization dedicated as much to the study of the physio-pathology of the tissues of the extremities as to the surgical correction of deformities should have a department with sections for clinical investigations of vascular, lymphatic, nervous, muscular, and bone disorders of the extremities with all the necessary clinical armamentarium; a section for experimental surgery with the appropriate animal house; sections for histopathology, micro-radiography, radiography, and photography, both clinical and experimental. This department should function in close liaison with the hospital which handles the clinical problems and houses the orthopaedic patients, and should be complemented by a library, lecture hall, museum, record offices, etc. Such a centre should be located in a university area in close connexion with other university departments such as those of inorganic and organic chemistry, pharmacology, physiology, etc., where any highly expert advice and help can readily be obtained when required.

It is not surprising, therefore, that when an opportunity arose for establishing such a centre, where the requirements of clinical medicine could be correlated with the strict discipline of laboratory research, this was seized. It was due mainly to the foresight of G. R. Girdlestone that such a centre was planned. Apart from the research potentialities inherent in a university centre so compact as Oxford, there are specially favourable opportunities for the investigation of orthopaedic problems in that city because, thanks to G. R. Girdlestone, clinical orthopaedics have been efficiently organized there for more than thirty years. The Wingfield-Morris Orthopaedic Hospital is thus a long-established centre drawing orthopaedic patients from a population of nearly 2,000,000. The first requirements for any investigation based on clinical material are an efficient method for recording and keeping the clinical data and that the analysis of these should be performed by workers of experience and objectivity. From such material the statistician, so recently praised by Sir Henry Dale,[5] must extract those factors which have real significance in the pathological process under study, without underestimating the importance of the individual case, which may sometimes throw as much light on a problem as the best and most copious statistics. It is from this sort of analysis that problems are isolated from the main body of observation and can then be individually studied and, when necessary, brought to the laboratory for experimental analysis.

The New Centre

Provisionally, with the help of the Nuffield Institute for Medical Research, Oxford, a beginning has been made in the working of such an organization, and some modest, if very urgently needed, building facilities are being provided to intensify the work at present undertaken. The Nuffield Orthopaedic Centre integrates into a working body both the Wingfield and its associated clinics, the Accident Service of the Radcliffe Infirmary, and the Nuffield Department of Orthopaedic Surgery. The first contact has been established between colleagues interested in poliomyelitis working in the Oxford Region, including doctors from the isolation hospitals, orthopaedists, neurologists, and research workers. As facilities increase it is hoped that they will combine to form a research group. A residence for postgraduate students has already been acquired, and the first foreign students are already working in the Centre.

To attract postgraduate visitors and junior members of the Centre a course of lectures is being given on Thursdays during term by experts on subjects which sometimes may seem to be outside the immediate interest of the orthopaedic surgeon. Discussions of current medical literature, also covering a wider field than that of pure orthopaedics, take place every month.

Plans have been drawn up for a suitable building (see illustration), and the money is already available; soon the facilities for trying this double-sided approach to orthopaedic problems will be increased once the erection of the first and smaller building is completed.

In recognition of the great life-work of Girdlestone, Lord Nuffield has given £10,000 to the Nuffield Orthopaedic Centre for the creation of a scholarship to be known as the Girdlestone Scholarship. This will be for the purpose of enabling doctors from overseas to spend a period of time at the Wingfield working within, and learning from, the organization Girdlestone created and which so clearly bears the imprint of his personality.

I have felt compelled to give this short account of the working and projects of the Nuffield Orthopaedic Centre as a last tribute to G. R. Girdlestone, the man to whom orthopaedics in general, and Oxford medicine in particular, owe so much.

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The Expert Committee on School Health Services met in Geneva from August 7 to 12, 1950 (*World Hlth Org. techn. Rep. Ser.*, 1951, 30), and prepared an outline of basic policies and approaches to the problems of establishing school-health services. To learn effectively it is essential that children should be really healthy, and health teaching is an all-important factor in their school life. The need for co-operation in planning between parents, community, professional groups, and so on was emphasized, and the committee approved the initiative taken by the W.H.O. Expert Committee on Professional and Technical Education in recommending the inclusion of mental health instruction in public health training. The importance of the teacher's role was stressed; the fundamental method required is continuous observation and interest in the child. The teacher alone can provide the physician and nurse with information vital to the understanding of the child's problem. Provision must be made for treatment of both physical and emotional health problems. In order to meet the needs of the schoolchild the health staff must be adequately trained: for instance, the physician must possess insight into the emotional needs of the child in addition to being a good clinician. The committee stressed the importance of continuation in child-health work; prenatal attention, infant-welfare centres, school-health services, and so on, should all be organized by the same authority or co-ordinated to ensure uninterrupted supervision.

ANTHROPOLOGY AND SEROLOGY

For some years now it has been clear that blood groups are valuable anthropological characters, since most of them occur in different proportions in different parts of the world. A considerable body of information about this exists but is almost inaccessible; much of it is buried among official records, and even the published work is written in a variety of tongues and scattered thinly among the many biological journals. On Saturday, March 17, at University College, London, the Royal Anthropological Society held a special meeting to discuss this difficulty. Serologists and geneticists read papers on blood groups in anthropology, and joined in discussing plans for a reference centre which should help to make blood-group data available to anthropologists.

The Mapping of Genes

Professor H. J. Fleure, who shared the chairmanship with Dr. J. C. Trevor, opened a crowded meeting by introducing Professor R. A. FISHER, who described some of the ideas and events which had made blood-group anthropology possible. It was now known that differences between races were genetically determined like those between children of the same family, and these differences could therefore be profitably studied by geneticists. Race was obviously an important fact, and the word no longer had so misty a meaning that scientists should be afraid to use it. When Professor Fisher became Galton Professor in 1933, the mapping of genes carried by normal human beings was progressing only slowly. The heredity of the ABO groups had been established by 1908, the MN and P blood groups had been recognized nearly 20 years later, and besides these only the "Taster" and "Secretor" characters, found in 1931 and 1932, were known. Professor Fisher, recognizing the need for more "marker genes" on which to base the study of human heredity, chose to use the Rockefeller funds at his disposal to create the Galton Laboratory Serum Unit. This unit (now taken over by the Medical Research Council) had been an important instrument in developing blood-group genetics. There were now twelve "markers" of use in human genetics, nine of them being blood groups, five of which were discovered within the last ten years. He emphasized this quickening tempo of discovery, and prophesied the identification of many more new blood groups.

Inbreeding and Blood Groups

Dr. C. D. DARLINGTON followed with a paper on "Blood Groups and Mating Groups," in which he discussed some genetical principles which must be considered by blood-group anthropologists. He first congratulated human geneticists on being able so easily to calculate and to map the frequencies of genes in populations; this was much more difficult for animal and plant populations, since most genes, unlike those responsible for blood groups, could be detected only by breeding experiments. Dr. Darlington then explained that major differences in the distribution of genes might be the result of the movement and mixing of populations; the distribution of group O people in Europe, for instance, seemed to have a historical explanation. However, it was important to remember that the movement of peoples might conceal the action of natural selection on the genes of small populations. People living in the same district tended to marry one another, so that human populations could be divided into inbreeding groups, though how large these were and how much they mixed was not known. Inbreeding would be expected to enhance the differences between such groups. In work on plants and animals geneticists had found that the same gene might be at an advantage in one population and at a disadvantage in another; for example, the gene responsible for group B might in one district be linked with a harmful gene, and become rarer there than elsewhere. Dr. Darlington suggested that an analysis, village by village, of blood-group frequencies might yield fascinating information on local or tribal variation.

The next two papers described work of this kind. Dr. J. A. FRASER ROBERTS reported an analysis of the distribution of the ABO groups in 52,000 blood donors living in the four Northern counties of England and the West Riding of Yorkshire. It had been at Dr. Darlington's suggestion that Dr. Fraser Roberts first looked among records of the Blood Transfusion Service for evidence of local variation. In a preliminary study some years ago, he had found indications of local differences among the Welsh and in Yorkshire. The structure of the population of North England, and also the completeness of the records, had made him decide on the present survey. He had classified donors according to their postal addresses, and had divided the region into 320 geographical units, each of which included at least 20 donors. The frequency of group A people varied widely from area to area, but these small units were easily grouped on the basis of this character into 19 regions, which differed significantly from one another but were internally homogeneous. In the Darlington region, for instance, group A people were only half as common as in the district west of Gateshead. The frequency of group B also varied, and 15 regions, which very surprisingly cut across the regions mapped for A, could be defined. The frequencies of A, B, and O among the 52,000 donors taken together were normal for North England.

Where Do the Welsh Come From?

Dr. I. M. WATKIN had followed the other line indicated by Dr. Fraser Roberts's preliminary survey in 1942. He had studied the ABO groups of 15,000 donors from Wales and 6,000 from the Marches. Industrial and mining communities had not been included. He had found a very high proportion of group O people in North Wales and in some isolated mountain regions further south. He hinted that this might indicate a distant relationship to the Berbers of North Africa, among whom group O was also very common; he added, more provocatively, that Welsh syntax had been thought to show the influence of an ancient element akin to the language of the white North African tribes. The distribution of the A gene also differed; Dr. Watkin had found patches where A was surprisingly common for Britain and approached the frequency found in Scandinavia. Several such patches, near Rhyl and Chester, for example, were known to have had Viking settlements. Another, a peninsula in Pembrokeshire, had been the subject of dispute, for authorities disagreed on whether or not Scandinavians had settled there. The most interesting of Dr. Watkin's results concerned the B gene. In the central moorlands he had found an unusually high proportion of B, and in one area the gene frequency reached 16%, or three times the average for Britain. In this area Professor Fleure had found traces of palaeolithic stocks, and it was therefore probable that the B gene, which used to be thought a late immigrant into Europe, had been present in Wales before the main stock of B came in from the East.

New Light on Early Population Movements

The last speaker, Dr. A. E. MOURANT, who has contributed so much to this field, began with a disarming apology for the enthusiasm of genetical anthropologists, who needed to remember that the techniques they used with such confidence had not yet superseded all others. His talk, which was illustrated by blood-group contour maps of the world, reviewed the conclusions which could so far be drawn.

The blood-group world could be divided into five regions, some more clearly defined than others. In Europe successive waves of immigration appeared to have brought in high proportions of O, A, and B genes in that order, and in the case of A there were traces of the route taken by the immigrants. There was some danger of over-simplifying the pattern, however; the wave carrying B had apparently arrived within the last 1,000 years, but other results besides Dr. Watkin's now suggested that group B existed among palaeolithic peoples. Yet among the Basques, who were supposed to be one of Europe's very ancient peoples, group B was only rarely found.

Continents and subcontinents could be distinguished by their characteristic mixtures of the many Rh types; it was interesting to find that local differences in these mixtures were rare and usually historically significant. There were traces of a Mediterranean set of Rh frequencies significantly different from those in Northern Europe. The Basques were apparently a relic of an ancient European population which was the source of the Rh-negative character, for Rh negatives were commoner among Basques than in any other people save one isolated Berber tribe. Berbers and Basques, Dr. Mourant suggested, might be related.

Africa was characterized by an Rh mixture unlike any other; there was no clue to whence it had originated, but the internal pattern suggested two main African stocks, a central and a peripheral.

Information about the rest of the world was more scanty and had not contributed much to anthropology. The separateness of Australasia was marked by the MN groups; and ABO, MN, Rh, and Duffy groups together underlined the isolation of the American aborigines without indicating their relationship to other peoples. Dr. Mourant's results showed that the new Kidd and Duffy groups, for which sera were still rare, would in time be valuable and sensitive anthropological tools.

Plans for a Reference Centre

In the afternoon a smaller meeting, with Miss M. L. Tildesly, in the chair, discussed plans for the setting up of a reference centre for blood-group anthropology. Among the speakers were Professor Fleure, Professor Fisher, Dr. A. Allison, Dr. Trevor, Dr. W. D'A. Maycock, and Dr. Mourant. On Professor Fisher's suggestion, it was agreed that this centre should be set up immediately. The meeting also agreed that a skilled person at the centre should have facilities for collecting and storing original data, cataloguing published work, and analysing results. The Royal Anthropological Institute is to appoint a committee to proceed with these plans.

THE MECHANISM OF HEARING

DR. HALLOWELL DAVIS'S LECTURES

When Helmholtz published his monumental work, *Sensations of Tone*, in 1863 he drew attention to an important and fertile field for investigation. But 50 years were to pass before there was any real development of this subject. In 1912 Adrian made an outstanding contribution to the study of nerve physiology by establishing the "all or none principle" which was to prove the foundation of the electrophysiology of nerve fibres, a subject to which Adrian and his associates have contributed unceasingly for the past 40 years. In 1930 Wever and Bray discovered the effect which has been named after them; the effect depends upon potentials developed in the cochlea that reproduce with great fidelity an acoustic stimulus applied to the ear. This discovery started a wave of investigation that has been spreading ever since. The recognition of the relationship between the "Wever and Bray effect" and the "all or none response" was a further valuable contribution, and both effects are constantly made use of in attempts to probe the secrets of the ear.

Dr. HALLOWELL DAVIS, director of research of the Central Institute for the Deaf at St. Louis, U.S.A., who has just been on an all too brief visit to this country, worked as a young man in Adrian's laboratory. Undoubtedly he must have been greatly inspired in his career by Adrian's influence, and no doubt his outlook was also affected by Wever and Bray's work. It is fitting, therefore, that Hallowell Davis's work should in its turn have stimulated the thoughts of countless physiologists, psychologists, physicists, and others working on deafness. During his visit to this country Dr. Davis delivered two lectures—the first on "The Effects of Noise on the Ear," at the Institute of Laryngology and Otology on March 20, and the second on "Recent Work on the Neurophysiology of the Cochlear Mechanism and its Bearing upon Clinical Problems," at the Institute of Neurology, Queen Square, on March 21. The Acoustics Group of the Physical Society was present at the second lecture.

Effects of Noise on the Ear

Dr. Davis deviated from the title of his first lecture to include an account of some new work on the problem of auditory theory, and particularly the problem of pitch. He discussed subjective experiments, which had been carried out after previous physiological work, that might throw light on certain curious effects that were observed in auditory fatigue, acoustic trauma, Ménière's disease, and other forms of nerve deafness. The effects of noise could be looked upon chiefly as modifications of delicate acoustical phenomena. He believed that much information could be obtained about faulty hearing and temporary acoustic trauma by paying close attention to subjective impressions. Dr. Davis introduced briefly the modern developments of Helmholtz's original theory and the frequency, or telephone, theory put forward about 1880 by William Rutherford, of Edinburgh. According to the "spatial theory," discrimination of pitch depended on the region of the basilar membrane excited by the stimulus, whereas the "frequency theories" supposed that the auditory nerve transmitted a time-pattern of impulses that simulated all the details of the auditory stimulus. Wever had recently put forward the "volley theory," in which an attempt was made to combine the two traditional views.

There seemed no doubt that the "place principle" did operate. The skilful experiments of Békésy demonstrated it directly. The observations of Guild and his collaborators had correlated high tone loss with pathological findings. More recently, Galambos, working in Dr. Davis's laboratory, had placed micro-electrodes in the medulla of cats and had been able to study the response in single neural units. He had found that each unit had a particular frequency to which it had a maximal sensitivity. In other words, the nervous elements were "tuned" as required by the place principle. Wever's modification of the frequency theory suggested that the brain made use of all the information about frequency which travelled along the nerve elements, and that there was no place effect below 1,000 c/s. Above 4,000 c/s he agreed that the place principle held entirely, and in the transition region from 1,000 to 4,000 c/s he believed that both place and frequency were effective.

Tone-pips as Auditory Stimuli

Dr. Davis described the technique of "tone-pips," which had been developed in his laboratory as an acoustic stimulus instead of pure tones. A tone-pip was a damped group of waves consisting of a few waves in which the tone began gradually, reached a maximum after three or four waves, and then rapidly died away. These tone-pips could be repeated at any desired recurrence frequency, and, if the period between pips was not less than 1/20 second, the nerve fibres had time to recover completely and fatigue in individual fibres was eliminated. The tone-pips had several advantages: (1) Nearly all the acoustic energy was concentrated in a band less than an octave wide, so that, according to the place principle, they activated a restricted region of the cochlear partition. (2) The relatively rapid onset allowed identification of the particular sound wave that initiated a nerve impulse. (3) At frequencies above 1,000 c/s only one impulse was set up in each fibre because of the rapid build-up and decay of the pip and the refractory period of the nerve fibre.

When listeners were asked to comment on the quality of the signal some very interesting results were obtained. At a basic frequency of 2,000 c/s and a recurrence frequency of 150 pips per second, nearly all listeners at first denied that the sound had any definite pitch and all were sure that the

frequency of 150 c/s was not present. Dr. Davis believed that this was because the impulses were travelling along fibres that were not associated with that frequency by the place principle. Listeners also agreed in describing such a sound as a "buzz," something like a knife blade rubbing on a gear-wheel. Various modifications of the basic frequency were tried. When the recurrence frequency was changed it was agreed that the sound or "wheel" could be described as "going slower or faster." When the basic frequency was changed, the effects were described as "small and metallic" for 4,000 c/s, "larger but still metallic" for 2,000 c/s, "like wood" for 1,000 c/s, and "like water" for 500 c/s.

It was difficult to assign any definite pitch, but when various attempts were made to compare the buzz with a pure tone for a recurrence frequency of 150 pips per second some gave 300 (plus or minus a few cycles) as equivalent, sometimes 450, 600, etc., almost never 150. The more musical subjects could specify the "key," but they were not sure which member of the harmonic series was most like the noise. Another group of "pitches" appeared that were related to the basic frequency of 2,000 c/s. Dr. Davis said he believed that whenever there was appreciable dissociation from the pure tone, or, alternatively, if a frequency was out of place on the cochlear partition, the sense of "buzz" or "roughness" appeared. The other aspect of sense of pitch he referred to as "body"; this was the contribution of the place principle. As a result of these observations Dr. Davis suggested a modification of Wever's theory, in which both frequency and place were effective below 4,000 c/s and in which place was the sole consideration above 4,000 c/s. In cases of acoustic trauma, having a dip in the pure-tone audiogram, the pitch might not be clear in the region of the dip; in other words, when the normal spatial distribution was interrupted a sensation of "buzz" was introduced. Some of the subjective impressions, he hoped, might give further clues in the theory of hearing. It was obvious that the central nervous system made full use of all the information offered to it through the selection of the nervous channels, and also in the frequency and synchronization of impulses in these channels.

Experiments on the Cochlea

In introducing his second lecture Dr. Davis showed slides illustrating the way in which he and his colleague, Dr. Fernandez, had inserted fine electrodes of 38 S.W.G. enamelled silver wire into the cochlea of the guinea-pig for experiments on its electrical behaviour. The animals were anaesthetized, and small holes were drilled into the scala tympani, scala vestibuli, and/or scala media of the basal and other turns. The entry to the scala media was the most delicate of these operations, as this scala contained the organ of Corti and was very susceptible to damage. The wires were sealed with dental cement where they passed through the bulla and the various electrodes connected to the separate channels of a 3-channel recorder. Two of these channels could be made to summate or to subtract their responses, if desired, by means of a change-over switch. The reference electrode was attached to the wound in the neck. As the cochlea of the guinea-pig protrudes into an air-filled bulla the electrical pathway from the reference electrode entered the cochlea chiefly by way of the internal auditory meatus, and was nearly equivalent to an electrode placed on the auditory nerve. Action potentials were apparently produced at the cell bodies of the spiral ganglion and not in the fine non-myelinated twigs. The cochlear microphonics arose in the organ of Corti, probably from the hair cells.

The results obtained from the various responses when acoustic stimuli were applied to the ear could be summarized as follows:

(1) The cochlear microphonic followed the wave form very closely at moderate intensities; it showed no refractory period.

(2) The action potential of the auditory nerve appeared as a negative electrical charge at all the cochlear electrodes.

(3) The action potential could be completely cancelled by subtracting the scala tympani signal from the scala vestibuli signal after adjustment of amplification.

(4) The cochlear microphonic was opposite in phase in the scala tympani and scala vestibuli respectively and could be cancelled by adding the signals.

By these methods action potentials of moderate voltage could be received and their latency measured, in spite of the simultaneous presence of a large cochlear microphonic which would otherwise obscure them. When this was done a second and smaller action potential was located, lagging 0.7 of a millisecond behind the main potential. This response came from the cochlear nucleus. Ignoring this secondary effect, some interesting results were obtained regarding the relationship between the timing of the incident sound waves and the electro-neural effects. Provided the stimulus was a pure tone it was found, in general, that there was not more than one nerve impulse per complete sound vibration. Dr. Davis said they wanted to determine what particular component of the mechanical vibration was responsible for the impulse; for example, was it displacement, velocity, or acceleration? The evidence so far appeared to indicate that excitation of the impulse was associated with the maximum velocity of the basilar membrane in the direction of the scala vestibuli. The number of impulses per second was limited, however, at high frequencies due to the nerve's refractory period.

As in his first lecture, Dr. Davis discussed the technique of tone-pips, which in this research were used at basic frequencies of 2,000 to 8,000 c/s at a recurrence frequency of about 20 times per second. In this way action potentials of the order of 250 microvolts were obtained. This form of stimulus was very useful in working out the relationship between the potentials and individual waves, and the results supported the evidence of timing previously mentioned. It also showed a minimum latency of about 0.6 of a millisecond. On reversing the phase of each wave in the group the action potential was found to shift, corresponding to about a half wavelength of the group, provided the basic frequency was less than 8,000 c/s. At 8,000 c/s, however, the change of latency was not observed; it was certainly less than 30 microseconds, and the results suggested that the nerve responded to the tone-pip as a whole and not to the individual waves. One might say the sense organ summated the energy in the waves. A second line of evidence for summation at high frequencies was found in the change of latency with the intensity of the tone-pip. Furthermore, a third electrical potential was identified as coming from the cochlea. This new potential showed the property of summation. The summating potential appeared to be located in the organ of Corti, as shown by measurement of its intensity at different points. It did not appear to have a refractory period and it outlasted the mechanical movement at high frequencies; in this way it behaved unlike the cochlear potential or microphonic. The potential was probably similar to the potentials recorded at the neuro-myal junction, to the post-synaptic potential of spinal neurons, and to potentials recorded from the muscle spindle of the cat. It was probably a general property preceding and initiating the real action potential. The summation potential might remain in the case of surgical damage or acoustic trauma after the cochlear potential had virtually or completely disappeared.

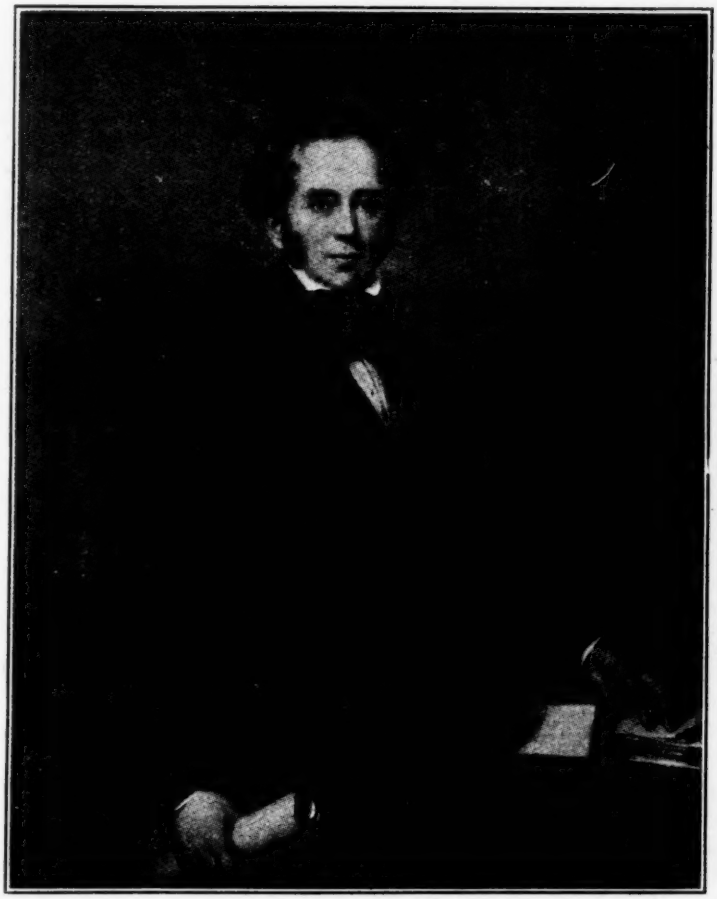
Finally, Dr. Davis discussed the perspective of the various neurophysiological effects. The cochlear microphonic was not a necessity for the development of action potentials; it was an accompanying phenomenon which might be an indicator of time and of intensity of movement of the organ of Corti. The summating potential was a necessary link in the process. To put it another way, neither the summating nor the action potential was in any way dependent on the cochlear microphonic.

A new blood group thought to be present in about 77% of Americans is described in *Nature* (March 24, p. 482) by Drs. F. H. Allen, jun., L. K. Diamond, and B. Niedziela.

WORCESTER AND SIR CHARLES HASTINGS

[FROM A CORRESPONDENT]

Sir Charles Hastings, the founder of the British Medical Association, is well entitled to rank as a prophet, but, the biblical saying notwithstanding, he has had honour in his own country. He was honoured by his fellow citizens as well as by the members of his profession during his life, and since his death there have been at least two outstanding occasions on which Worcester has joined with medicine in tribute to his memory. One of these was at the jubilee and the other at the centenary of the Association, and now a Sir Charles Hastings Memorial Festival is to be held at Worcester on May 30, when a memorial lecture will be delivered by Dr. W. H. McMenemey, preceded by a service in the cathedral at which the Bishop will give an address.



Hastings was not a native of Worcester—he was born in Shropshire—nor did he die in the town, but it was there he did his lifework, and he was physician to the infirmary for 44 years. When he was 18, with no medical qualifications beyond apprenticeship for a year or so to a medical man, he offered himself for the post of house-surgeon, his competitor being a well-qualified local surgeon. The election was by the governors, who numbered 300, and Hastings, on horseback, canvassed every one of them. In the result he secured the appointment by 134 votes to 133. But his supporters never regretted their choice, and six years later, having meanwhile obtained his medical degree in Edinburgh, he was appointed at the age of 24 to the post of physician, a post which he held to within four years of his death. In Worcester he did some remarkable work. He was not at all content to be an ordinary country practitioner, and he so impressed himself on the townspeople that when Worcester was threatened with an outbreak of cholera the mayor and corporation invested him with almost dictatorial powers, and he issued drastic orders in the matter of sanitation and the removal of certain of the inhabitants, with the result that the plague was stayed.

The Provincial Medical and Surgical Association

It was in the board-room of the infirmary, where visitors to the forthcoming Festival will see an exhibition of Hastings relics, that on July 19, 1832, he founded the Provincial Medical and Surgical Association. It was there that he delivered his inaugural address, which was described in a resolution as "an able and luminous discourse" and ordered to be printed and sent to every member of the new association and to form the introductory article to the first volume of the *Provincial Medical and Surgical Transactions.*

Only on two subsequent occasions was the annual meeting of the Association held in its city of origin. The first was in 1849, when Hastings himself was president, and the second, in 1882, was the jubilee meeting. At the jubilee meeting Sir Charles's son, Mr. G. W. Hastings, M.P., himself a pioneer of medical reform and adviser on that subject to the Association, gave an interesting account of his father's career. Another event was the presentation to the city by the Association of a bust, which was placed in the Victoria Institute Public Library.

The Association after this became too large to have its annual meeting accommodated in a town as small as Worcester, but at the centenary in 1932 a large number of members—a special train was filled with them from London—went on pilgrimage to Worcester, headed by the president, the late Lord Dawson of Penn. The first of many events on that day was the unveiling of a Doulton tablet on the front of the house, No. 43, Foregate Street, in which Hastings had lived and carried on his practice (by this time it had become a furnishing establishment). One Worcester alderman stated that he remembered seeing as a boy the long line of carriages of private patients waiting outside that house on certain afternoons. The pilgrims then went to the cathedral, where a memorial window, given by the Association, was unveiled by Lord Dawson and dedicated by the Dean. The window depicts St. Luke in the centre, and on either side a representation from the parable of the Good Samaritan. On the same occasion the Hastings portrait, which was a family possession, was formally presented to the Worcester Division, the condition of parting with it being that a replica should be painted for the Hastings descendants, and this was done by a talented lady of the Hastings family. The pilgrimage was attended by several members of the Hastings family, one of whom, a grandson of Sir Charles, gave an address. The Hastings family was extensive and was said to be connected by cousinship with Warren Hastings, the first governor-general of British India. Charles Hastings himself was one of a family of 15, and one of the 15 was a father of 10. Hastings himself, however, had only one son and one daughter. It was also a long-lived family, with more than one centenarian in its tree, but Charles Hastings died, of duodenal carcinoma, at the age of 72. His grave in Astwood cemetery, on the summit of Sunrise Hill, was also visited by the pilgrims at the centenary. The tombstone was restored by the Association out of the Sir Charles Hastings Fund.

Medicine in the Provinces

George Eliot, the novelist of the Midlands country, where she lived in the 'thirties and 'forties of the last century, may

well have had some such physician as Hastings in mind when she wrote *Middlemarch*, for she put into the mouth of one of the characters the words, "A born provincial man who has a grain of public spirit as well as a few ideas should do what he can to resist the rush of everything that is a little better than common towards London. Any valid professional aims may often find a freer, if not a richer, field in the provinces." It will be remembered that Middlemarch supported two physicians, whose fee was a guinea, as well as a number of surgeons and apothecaries.

The British Medical Association at its start had a pronounced provincial bias. Hastings wanted to see utilized the valuable clinical material in the provincial hospitals, and to secure co-operation in the provinces for the advancement of medical science. From its earliest days the Association was representative not only of general practitioners but of physicians and surgeons to provincial infirmaries. Its object, explicitly stated by Hastings, was the maintenance of the honour and respectability of the profession generally in the provinces. How it invaded the capital and made its headquarters in London is another story. But it is well sometimes to go back, in spirit and even in body, to the town by the banks of the Severn where it had its beginning.

Reports of Societies

SURGERY OF THE HEART AND GREAT VESSELS

The surgery of the heart and great vessels was discussed on April 4 at a meeting of the Section of Surgery of the Royal Society of Medicine, to which the Section of Medicine had been specially invited.

Professor C. CRAFOORD, professor of thoracic surgery at the Karolinska Institutet, Stockholm, opened the discussion, confining his remarks to the surgical treatment of coarctation of the aorta and patent ductus arteriosus. Both these conditions could be diagnosed with a high degree of accuracy by simple bedside methods. Cardiac catheterization and angiocardiography were required only in order to pick out rare cases imitating patent ductus arteriosus, such as aorto-pulmonary septal defects, and the few cases of coarctation of the aorta (about 10%) that were unsuitable for surgery on account of the anatomical nature of the stricture.

In Stockholm they paid special attention to selective angiocardiography, whereby the dye was introduced directly into that part of the cardiovascular system which required studying, so that contrast medium elsewhere did not obscure the view. Selective angiocardiography might be in the form of retrograde aortography, the dye being passed directly into the aorta via the radial artery, or the dye might be injected through a large catheter inserted into the pulmonary artery.

Coarctation of the Aorta

Out of 365,000 mass skiagrams, coarctation of the aorta had been demonstrated in 27, which gave an incidence of 1 in 13,000. If the skiagrams of subjects over 50 years old were excluded, on the grounds that 90% of cases of coarctation died under the age of 50, the incidence became 1 in 7,000.

Professor Crafoord had now operated on 75 patients with coarctation during the six-year period 1944–50. Of these, the majority first developed symptoms between the ages of 10 and 25; 15 began to have symptoms between the ages of 5 and 10, and 10 after the age of 25.

Direct aortography had been performed in 75 cases with no deaths, and this technique had served to prevent 10 patients from having an unnecessary thoracotomy. He said that they had had only one death in over 1,000 angiocardiograms, and one death in many times that number of cardiac catheterizations.

He performed an end-to-end aortic suture in the great majority of cases, and was technically satisfied if the site of repair was shown to be 60% of the diameter of the rest of the aorta, for a complete functional cure could then be expected. Subsequent aortograms revealed the success of the procedure not only by outlining the site of repair but also by showing disappearance of collateral channels. He did not wish to discuss the value of aortic grafts, but thought that this was a very interesting development and must await further research. He had had six deaths in 85 operations, three from complications of the aortic suture, two because of acute bleeding elsewhere, and one from the unexpected presence of periarteritis nodosa. Of 24 patients followed up for five years or more, 17 were completely cured. It seemed clear that a repair carried out in childhood enlarged with the aorta in a natural manner as age advanced. Early operation was therefore desirable.

Patent Ductus Arteriosus

Professor Crafoord had operated on 282 cases of patent ductus arteriosus with 10 deaths. There were only two deaths in 266 straightforward cases. In 16 patients, however, there had been marked pulmonary hypertension, and eight of these died; moreover, such pulmonary hypertension had persisted in some of those cases that were successfully ligated. He felt that double ligation was the method of choice if the ductus was long enough to permit it and if the diameter of the duct was less than 40 mm. He had had three cases showing recanalization, and in two of these the ductus before operation had been more than 40 mm. wide. He had divided the ductus in 47 instances, usually when it was very short and wide. One of these had recanalized. If patients with marked pulmonary hypertension were excluded, the mortality rate was under 1%, and he felt that the long-term morbidity and mortality rates were much higher in the non-operated group.

Pulmonary Valvulotomy

Mr. R. C. BROCK spoke about direct cardiac surgery. He had now performed 130 such operations—that is, either pulmonary or mitral valvulotomy or infundibular resection. These operations could not be regarded as "stunts," but had come to stay; they required good team-work.

There was no question about the value of pulmonary valvulotomy in cases of pure pulmonary stenosis with or without reversed interatrial shunt. But time alone would show how pulmonary valvulotomy compared with the anastomotic operation in cases of Fallot's tetralogy with valve stenosis. He felt that it was a more physiological operation, and he insisted, from his own experience and from the figures of Keith, of Brown, and of Sellors, that valve stenosis occurred in about 40% of all cases of Fallot's tetralogy. He had undertaken pulmonary valvulotomy in 28 cases of pure pulmonary stenosis and in 29 cases of Fallot's tetralogy; there had been 10 deaths, eight in pulmonary valve stenosis and two in Fallot's tetralogy. There had been only two deaths in the last 37 cases, and only one in the last 29. It was only fair to say that four of these deaths occurred under anaesthesia before he had touched the heart and in one case during induction.

The risk was far greater in patients over 20 years old. The oldest patient with pure pulmonary stenosis had been 29, the youngest 14 months. The ages of the patients with Fallot's tetralogy had ranged between 3½ and 24 years.

Of his last 50 cases of Fallot's tetralogy 21 (42%) had valve stenosis. When the stricture was infundibular it might be high, intermediate, or low, and was usually linear or membranous and therefore also suitable for the direct attack. He had performed infundibular resection in 24 cases, with seven deaths. In six patients, combined valvulotomy and infundibular resection had been successfully carried out.

Mr. Brock stressed how greatly the heart tolerated interference. Three factors certainly contributed to success: (1) Simplification of the operative procedure. (2) The administration of adequate oxygen by the anaesthetist.

(3) The proper use of procaine intravenously, into the pericardial sac, and as a local anaesthetic into the heart muscle at the site of the incision in the right ventricle.

At the end of his talk Mr. Brock showed an excellent film illustrating the whole procedure of pulmonary valvulotomy. The lesion of pulmonary stenosis consisted of a conical membrane with a small hole in the middle. The object of the operation was to split the membrane so that two cusps were formed which were functionally efficient. Secondary pulmonary incompetence had not occurred in any case. Haemorrhage at the site of the incision in the right ventricle was controlled digitally. A special valvulotome was passed through the right ventricle and was guided into the pulmonary valve by hand. Bougies of increasing width were passed subsequently to increase the splitting, and finally a special expanding dilator was inserted which would open up to a maximum of 2.5 cm.

Mitral Valvulotomy

Mr. Brock went on to discuss mitral valvulotomy, which he regarded as a much more important subject in view of the frequency of mitral stenosis and the type of individual affected. He felt that operations on cases of congenital heart disease were probably best undertaken at a few special centres, but it was highly desirable that all thoracic surgeons should tackle mitral stenosis, for there were far too many cases ever to be dealt with at special centres alone. There had been three stages in the development of mitral valvulotomy: the first was 25 years ago, when nearly all cases treated surgically died and the courageous attack by the pioneer surgeons suffered a bloody defeat; the second was four to five years ago, when the speaker experienced great difficulty in getting started, operating on only eight cases in two years; finally, there was the present situation, which was characterized by irresistible pressure from the patients themselves—so much so that routine cases of mitral stenosis on the waiting-list for valvulotomy tended to remain on that list month after month because emergency cases on the brink of acute pulmonary oedema had to be given priority.

To date he had carried out 48 mitral valvulotomies, with eight deaths; but there had been no deaths among the last 24 cases, and these included some that were extremely severe. Patients under 20 were considered unsuitable in view of the likelihood of their not being free from further rheumatic activity. He preferred patients under 45 years of age, but had operated upon one at 50. About half the patients had calcified valves, but this had not proved awkward. Auricular fibrillation had been present in 21 cases, five of which had died. Post-operative auricular fibrillation had occurred in eight patients but had persisted in only three. Systemic emboli and intra-auricular clotting were not considered contraindications to operation.

In the 40 patients that had survived, the results had been good or excellent in 37 and poor in three. Pulmonary hypertension appeared to diminish greatly subsequently. For example, one patient with a pulmonary artery pressure of 130/56 was re-catheterized six months after valvulotomy, when the pressure was found to have fallen to 40/10. At the present time there were insufficient physiological studies post-operatively to warrant any dogmatic statement on such points. There was, however, no doubt at all that the operation had thoroughly justified itself. Present work was really concerned with defining and extending the criteria on which a proper selection of cases could be based and extending the pre- and post-operative clinical and physiological assessment.

Selection of Patients for Operation

Dr. MAURICE CAMPBELL reminded the meeting that accurate diagnosis was not always as easy as might have been thought from the excellent angiocardiograms of the previous speakers. Interpretation of angiocardiograms and physiological studies was sometimes very difficult, but there could be no doubt about their value.

He said that there were always two chief points to consider in cases of mitral stenosis: (1) How much of the disability was mechanical, resulting from the valve disease; and (2) how much of it was the result of myocardial disease. Obviously the cases likely to do best were those with maximum mitral stenosis and minimum damage to the heart muscle, and these were particularly cases with cardiac asthma and pulmonary oedema. The most important contraindication to valvulotomy was rheumatic activity. Neither mild aortic valve disease nor a mild degree of mitral incompetence was a contraindication; gross mitral incompetence was another matter. He confirmed Mr. Brock's contention that mitral incompetence did not result from the operation, and also that pulmonary incompetence did not result from pulmonary valvulotomy as performed by Mr. Brock. Another contraindication to the surgical treatment of mitral stenosis was congestive heart failure, for this usually meant a bad muscle or a case that was too advanced.

Since the first successful mitral valvulotomy in 1948, two and a half years had elapsed, and it was already clear that improvement had been maintained in all cases followed up. There was no question of a quick relapse. There was some evidence that pulmonary hypertension was reversible in these cases, and sometimes the fall in pulmonary artery pressure was gradual rather than abrupt. He agreed with Mr. Brock that mitral stenosis should be tackled surgically by all thoracic surgeons, as the problem was far too big for a few special centres. Success depended upon a very close co-operation between physician and surgeon.

Dr. Campbell then discussed the surgery of congenital heart disease. He found it difficult to advise parents whether a child with coarctation should be operated on or not. There was no doubt that many of these patients did relatively well if left alone, although disastrous complications might occur sooner or later. On the other hand, the surgical mortality rate was 10%, another 10% were found to be inoperable, and a third 10% were not greatly improved. These were not very encouraging figures to offer a patient who seemed well and active at the time. He found it less difficult to advise about patent ductus arteriosus, but a 2 to 3% mortality rate was still a drawback to operation when life expectation was 20 to 30 years and the patients were physically active and felt well. Routine ligation could be advised when the surgical mortality rate reached 1%. For similar reasons he advised ligation rather than division of the ductus. With regard to Fallot's tetralogy, Dr. Campbell pointed out that the Blalock operation gave excellent results in 80% of cases and a mortality rate of 10%. It had been proved that pulmonary valvulotomy was capable of producing just as good a result as the Blalock type of anastomosis, but he was not yet certain in what percentage. Theoretical considerations about which might be the better procedure were fallacious; time alone would show.

The *Annual Report for 1950* of the Health Branch of the Government of British Columbia among much other information describes the difficulties encountered in collecting information about births, marriages, and deaths among the Indian population, since for many generations Indians have changed both their given and their surnames at will. Apart from attempting to educate them to stick to one name, many indirect methods have therefore to be used—for instance, by studying the annual enrolment of new Indian pupils in schools. A check of the roll in 97 schools last year showed that there were errors in 55% of the school rolls compared with birth registrations and agency nominal rolls. The Doukhobors, a curious Ukrainian sect which emigrated to Canada in 1899, also gave much trouble, since one group, known as the Sons of Freedom, stubbornly refuse to obey the laws regarding vital statistics, and in general they are said not to understand the importance of accepting a legal form of marriage. In spite of these difficulties, the population of British Columbia is now estimated at 1,138,000. The Tuberculosis Control Division reports that 1,713 new cases were discovered, and that there has been a marked drop in the mortality and morbidity of this disease during the year.

Correspondence

Hexamethonium in Hypertension

SIR,—Drs. S. Locket, P. G. Swann, and W. S. M. Grieve (April 14, p. 778) are to be congratulated on their presentation of a very important body of work on the management of hypertension, on their critical attitude which will temper over-sanguine expectations in the minds of those lacking their experience, and on their emphasis on the possible importance of the ion with which the methonium is combined.

Dr. Gavin Shaw and I have for fifteen months been using hexamethonium bromide, orally administered to ambulant patients, and our earlier patients have been continuously on methonium for this period of time. On the whole, our results (which should shortly be published) have been more satisfactory than those of Locket, Swann, and Grieve.

A hypotensive effect, lasting as long as six hours, may be obtained by a single oral dose of methonium. Since this effect is obtainable with the first dose administered, it can have nothing to do with a bromide effect. By suitable spacing of the dosage, it is possible to achieve an almost continuous lowering of the blood pressure. We have rarely been able to give much more than 3 g. per day without reduction of blood pressure to a disabling level. Adjustment of dosage is not easy, because the margin between an ineffective and a disabling dose appears to be small. On effective dosage, the patients always show a degree of postural hypotension. It may well be that, just as after a successful sympathectomy, this postural hypotension has an important effect in diminishing the strain on the heart and vessels. Moreover, even though it be impossible with methonium to produce an uninterrupted reduction in blood pressure, it is reasonable to suppose that the lowering of the pressure for several periods of a few hours in the course of the day may be beneficial.—I am, etc.,

Glasgow. W. A. MACKEY.

Hiccup and Hexamethonium

SIR,—Any effective therapy directed towards intractable hiccup is welcome, and for that reason I am prompted to communicate the following résumé of a case recently referred to me.

A male, aged 76, had suffered from epigastric pain ½ to 1 hour after meals since recovering from influenza one month before. On February 16, for no obvious reason, hiccup set in and persisted despite the usual orthodox treatment, including paraldehyde, morphine, CO_2 inhalations, and pressure on the eyeballs. Haematemesis occurred on February 23, and the patient was admitted to hospital on the following day. There was no repetition of the haematemesis in hospital, but hiccup continued. Routine clinical examination failed to reveal any abnormality to account for this distressing symptom. On February 26 treatment with hexamethonium bromide by mouth commenced. Two tablets, each containing ¼ g. hexamethonium bromide, were given with no result, but four hours later three tablets were given. Half an hour later complete relief was obtained. There has been no recurrence. A subsequent barium meal failed to reveal any abnormality in the gastro-intestinal tract, and the blood urea was 42 mg. per 100 ml.

The aetiology of the hiccup is uncertain, but the dramatic and immediate response to the exhibition of hexamethonium bromide was such that, since persistent and intractable hiccup does not come the way of any one physician frequently enough to test the efficacy of a new preparation, this report is communicated so that others may be prompted to test it further in similar cases. The physiological action is due to ganglionic blocking. No adverse side-effects were observed.—I am, etc.,

Lymington, Hants. R. J. MCGILL.

Enlarged Prostate

SIR,—Three years ago I was consulted by a man aged 77 who said he had not passed water for 20 years. He had catheterized himself daily throughout that period, and at the consultation complained of irritation in the bladder. At that time he had the appearance of good health, and his urine was not even hazy. When asked if he sterilized his catheter, he replied, "Yes, once a week." In due course by the transvesical route I removed with the diathermy needle a mass of obstructing fibrous tissue from the prostatic region, which procedure enabled him subsequently to pass his water with ease. I am now informed by a relative that at the age of 80 he is in excellent health and very active: he walks four to six miles a day.

The claim that success from catheterization depends on a rigid routine of asepsis is of course not true, as the above case and that of Dr. D. I. Evans (April 14, p. 819) show. Moreover, many other cases have gone the wrong way in spite of meticulous observance of an orthodox ritual. There are in fact many circumstances that conspire to decide the course of events; and, while we cannot always foretell the consequences of prolonged intermittent catheterization, we can rightly indicate a bad prognosis for some. Certainly the majority of cases do badly on this treatment.—I am, etc.,

London, W.1. H. P. WINSBURY-WHITE.

Unusual Accident

SIR,—The following note may be of interest as indicating a possible danger from zip fasteners.

A patient aged 26 was admitted to a military hospital with the ventral part of his prepuce firmly caught in the zip fastener of his civilian sports trousers. Several attempts had been made to free him at his unit sick quarters without success. By snipping out the stitches from the seams the fastener was released from the trousers. Under a procaine ring block a further unsuccessful attempt to release the prepuce, now bruised and swollen, was made. A circumcision was therefore performed in the usual way and there was an uneventful recovery.

A search through the *Quarterly Cumulative Index* has failed to reveal a similar case.—I am, etc.,

H. ELLIS,
Capt., R.A.M.C.

Visual Hallucination of the Self

SIR,—Are autoscopic phantoms likened by Professor J. Lhermitte to mirror images (March 3, p. 431) because of their incorporeal quality or because they are laterally transposed? If the latter condition applies, Féré's patient with right-handed paralysis should have seen his phantom minus a hand on his (the patient's) left. If there were any differential features to determine the point, the man who saw phantom back-views of himself should have seen them *not* transposed, since his mental impression of his appearance from the rear could have been formed only from doubly reflected images such as one sees through two mirrors in the tailor's fitting-room. This line of reasoning might help to convince a patient that a Doppelgänger is not an "astral body" but a subjective phenomenon "arising from the heat-oppressed brain."—I am, etc.,

Birmingham. B. R. SANDIFORD.

Breast-feeding

SIR,—Being a mother and a doctor, I would like to say how thoroughly I agree with the views expressed by Dr. Charlotte Naish (March 24, p. 607). There are one or two points I wish to make.

First, Dr. Naish criticizes putting the baby to the breast within the first few hours of delivery; when this is done in order to "teach it to suck" it does seem senseless and futile, but surely the more orthodox reason given is that it causes contraction of the uterus; from personal experience I can say that such is very definitely the result and only about one minute's sucking is needed. If the baby was shocked at delivery it would seem best to dispense with the suckling for the first day or two.

Secondly, the congestive phase of the breasts is too often neglected; the medical staff may be unaware that such exists, and the nursing staff knows only one treatment—i.e., supportive binding of the breasts. I feel certain Dr. Naish is right when she says complementary feeds, when necessary, should be given with a spoon and not the bottle; the extra trouble is well worth while.

Finally, I would like to make a plea that when test-weighing is done during the puerperium it should be done without the mother's knowledge if possible; I have been appalled by the anxiety and near hysteria shown by normally sensible women over these four-hourly reports.—I am, etc.,

London, N.W.6. FREDA S. REED.

Toxic Chemicals in Agriculture

SIR,—It is indeed gratifying that the B.M.A. has interested itself in this vital subject, but we cannot let pass without challenge the statement which appears in the first line of the memorandum (March 24, p. 639) recently circulated to members of the medical profession to the effect that the said insecticides and weed-killers are *essential* for the production of our crops. If this is indeed so, then Nature has slipped up very badly in failing to make them available to mankind before the twentieth century. Moreover, to make such an assertion is to set aside what may very well prove to be one of the most vital pieces of research of the present century —i.e., the work of Sir Albert Howard, who has demonstrated, to our satisfacton at any rate, that pest incidence in agriculture is a measure of the biological unbalance of the soil and that the remedy is to restore the correct balance with live humus.

Furthermore, while we are warned to be on the look-out for possible cases of poisoning among the relatively few workers who carry out the actual spraying operations, no word appears about the possible effects of the resultant food on the consumer. Again, if we are to accept the evidence provided by Sir Albert Howard and the closely related work of Sir Robert McCarrison, the fact that a crop is pest ridden is an indication of soil deficiency, which means that in turn the resultant product will be deficient in nutritional value. Is it not serious enough in itself that the public must tolerate deprived crops without adding the risk of poisoning the same?

We make the plea, Sir, for a much wider vigilance in this matter and a less ready acceptance of the inevitability of the use of diseased methods to deal with disease caused by human improvidence.—We are, etc.,

I. A. MACDOUGALL.
Bournemouth. K. VICKERY.

Drug Eruptions

SIR,—In the Refresher Course article of April 14 (p. 809) there is omitted the most topical drug of all—*p*-amino-salicylic acid. This, in my experience, gives rise to a generalized small red papular eruption, together with several small erythematous patches on the face. The rash is associated with high temperature and vomiting. It disappears in a week after the use of antihistamines internally and calamine lotion externally.—I am, etc.,

Glasgow. J. KELVIN.

Baths for Maternity Patients

SIR,—The shortage of pupil midwives in maternity hospitals and institutions threatens to cause a major breakdown in the maternity services, and already has increased the burden on the existing staff. It is particularly important, therefore, that the consultant obstetricians review the practice in their wards, so that all unnecessary procedures in the nursing of patients are eliminated. The purpose of this letter is to draw attention to one matter which will ease the burden for the existing staff. It is that all normal patients, even though they have had an episiotomy or a perineal tear, should be allowed baths from the fourth day. This has been my practice for some years now; it has the supreme advantage that perineal swabbing becomes unnecessary after the fourth day (it may be necessary to give the patient two baths on the fourth day, but thereafter one bath seems to be sufficient); the patients like it; any trifling infection that may be present is washed out of the way and the risk of cross infection in the hospital seems to be reduced; and from my experience the sisters and nurses are delighted. I do not recall seeing a patient who had suffered because of this practice, and I commend it to your readers.—I am, etc.,

Sheffield. C. S. RUSSELL.

Non-specific Cervicitis

SIR,—In commenting on Dr. Margaret Jackson's paper on cervicitis Dr. Jelinek (March 17, p. 585) states that he has "yet to learn in what way non-specific cervicitis of the type commonly seen in gynaecological departments differs pathologically from non-specific cervicitis in other departments." From experience in a sub-fertility clinic I can say that there is such a difference, the main one being that the cervicitis is usually symptomless. Patients in a gynaecological department usually complain of backache, heavy feeling in the abdomen, menorrhagia, dyspareunia, or leucorrhoea, whereas among sterility patients these symptoms are commonly absent and the patient may deny any excessive discharge even when, on examination with a speculum, the cervix, at all phases of the cycle, can be seen bathed in pus, though more usually the condition is not so extensive. In a series of 205 cases there were 108 cases of cervicitis, or 54%. It has been found in this clinic that some 10% of these cases harbour pathogenic bacteria, of which the most common are *B. coli* and haemolytic streptococci. A second series of 42 patients, all mothers and presumably fertile, who came for contraceptive advice, was used as a control, and in no case was any pathogen cultured.

It would seem, therefore, that the pathogens may be of significance in relation to the sterility, and in fact this is proved by the frequency with which conception occurs after treatment directed at the specific organism, and after cauterization.

In no case of the 205 cultured was a gonococcus isolated, and in fact in the whole series of cases the history of old infection with venereal disease has not been higher than the 4% quoted by Sutherland as being the accepted incidence of venereal disease in the total population.

I have to agree with Dr. Jackson, therefore, that there is a distinct difference between the cervicitis which brings a patient to a gynaecological department and the type of cervicitis discovered in a sterile woman, as the only symptom in the latter may be an interference with her biological function of becoming pregnant.—I am, etc.,

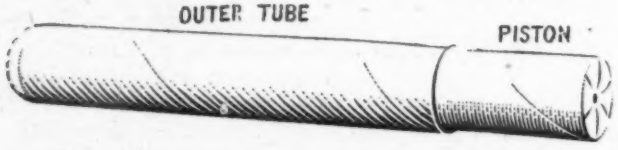
Manchester. B. SANDLER.

Applying Jelly to the Cervix

SIR,—For some time I have felt the need for a more efficient means by which a patient can apply local medication in the follow-up treatment of cervicitis and vaginitis. Reliance has been placed in the past upon the insertion of pessaries by an untrained hand, with the risk of additional infection. The pessaries are often not placed high enough to be effective, and with some pessaries leakage causes distress. These difficulties often drag out treatment for months. Medicated jellies applied by means of washable syringe-type applicators overcome some of these difficulties, but the cleansing of such applicators cannot safely be entrusted to unskilled or unreliable patients. Disposable applicators to be used once only solve these problems. Various such applicators supplied already charged with specific medicaments—e.g., sulphathiazole jelly or solid pessaries—have been used abroad (Siegler, *Amer. J. Obstet. Gynec.*, 1946, 52, 1).

I have had designed for me a disposable applicator illustrated here for use with a variety of medicated jellies or ointments as required. This applicator consists of an outer

tube (length 95 mm., diameter 15 mm.) made from smooth white spirally wound paper into which is fitted a closed inner tube (piston) made of the same material and held in the withdrawn position by a small notch in the outer tube. The jelly or ointment is squeezed from a collapsible tube into the open top of the applicator. A small aperture provided in the piston top prevents the formation of an airlock and the space in the outer tube (capacity approximately 6 ml.) can thus be completely filled. The patient inserts the full length of



the outer tube into the vagina and presses the piston home, expelling the jelly into the vaginal vault. The applicator is withdrawn and discarded. It may be thrown into the lavatory, since it disintegrates in water. With the applicator I have employed an inert jelly base consisting of 6% ethylated hydroxy-ethyl cellulose in distilled water and compounded with the usual agents—e.g., acetarsol, lactic acid, silver picrate, boric acid, ichthammol. The jellies are well retained, spread readily, mix with the vaginal contents, and inserted in this way reach the vaginal fornices. Hence they need not be applied as frequently as the corresponding pessaries. The method has been thoroughly tested during the past year and patients find the procedure quite easy. Applicators and jellies can be obtained from Messrs. Kylon Ltd., London.—I am, etc.,

London, W.1. MARY BARTON.

Industrial Health Investigation

SIR,—Commenting on your annotation on silicosis in foundry workers (March 10, p. 520), where you suggest that inconvenient physical examinations may contribute to a workman's reluctance to be examined in industrial health examinations, Dr. R. S. F. Schilling (April 7, p. 759) replies that it appears it is the investigators and not the industrial workers who must be blamed for incomplete surveys. I entirely agree. He quotes a refusal rate of less than 2% in a recent survey into the incidence of peptic ulcer among more than 1,000 employees, while in Manchester his own experience is a 3% refusal among over 300 cotton workers.

In a two years' clinical and radiological survey, which I carried out recently into the incidence of silicosis among stonecutters in the granite industry in Aberdeen (not yet published), the response was in keeping with these surveys. Of 521 men on the nominal rolls, three men, while anxious to co-operate, were by reason of old age and severe arthritis physically unable to appear for *x*-ray examination. Of the remaining 518, only eight (or 0.9%) actually refused to come forward for examination. With one exception all who refused were elderly men aged 65 and over, who quite obviously felt that they had silicosis and argued that they themselves had nothing to gain from submitting to examination. Furthermore, of 33 retired stonemasons all appeared for *x*-ray examination.

While agreeing with Dr. Schilling that the success of such surveys depends largely on individual approach to management and men, supported by trade unions, I wonder how much depends on a changed attitude to health in the lay mind?

Professor E. L. Collis, formerly of the factory medical inspectorate, carried out a survey similar to mine in Aberdeen in 1909. The results, unfortunately, were never published, but an excerpt remains of his address to the men 38 years ago.

"We are doing our best, and you must not think you have just got to go on doing your work and get everything done for you. It is not fair. I must say these things emphatically, because I found when I came to Aberdeen to examine the granite workers . . . I had more opposition from men here in getting them to come to me to be examined and to let me look at their chests than I have known in any part of the United Kingdom. It was most discouraging and disappointing, and I ask you to change that spirit if you want to get rid of consumption from your midst."

This provides an interesting comparison of fathers and sons, showing, I think, that in its attitude to preventive medicine public opinion has undergone a considerable change over the intervening years.—I am, etc.,

Aberdeen. ALEX. MAIR.

Exchange Transfusion Methods

SIR,—We were very interested in Dr. M. S. Fraser's letter (March 3, p. 475). As the neonatal sick unit in which we work takes in infants from a wide area, some cases are received too late for the umbilical vein to be of use. The technique of Weiner and Wexler, in which the radial artery is cut, was therefore used in these cases, and it was found to be both simple and effective. After a few cases it was found that the use of heparin could be avoided by intubating the radial artery with polythene tubing. The tubing leads from the radial artery into an M.R.C. transfusion bottle, so that the rate of drip of the exsanguinated blood can be observed. The input flow of blood can then be adjusted to approximately the same rate (the size of drop is larger in the citrated blood). A special scale graduated in millilitres is attached to both bottles and shows at a glance the intake and output of blood. In cases where the umbilical vein is patent it is used in preference to the saphenous vein, but the radial artery is always used for exsanguination. In this way a pint of blood can be exchanged in six to eight hours.

We believe that an exchange transfusion carried out in this way has less risk for the infant than one in which constant manipulation is required and where 30–40 ml. are being rapidly injected and extracted from an infant whose cardiac muscle may be affected by anoxaemia. We have never seen the tying of the radial artery cause any ill effects.—We are, etc.,

C. M. B. FIELD.
Belfast. E. HAWKINS.

Operating Theatre Technicians

SIR,—Few will agree with Mr. David Aiken (April 14, p. 820) in his opposition to the introduction of operating theatre technicians. So many of these men served as operating room assistants (O.R.A.s) in the R.A.M.C. and other services in the late war, and are thus entitled, if for no other reason, to their places in peacetime hospitals. War surgeons will recall with pride and gratitude that little band of O.R.A.s who stood by them in those trying days overseas, and who gave an example of team spirit and sacrifice which might well be emulated in our hospitals to-day.—I am, etc.,

Longforgan, Perthshire. MARTIN FALLON.

SIR,—Our letter of February 24 (p. 417) was a plea, from the anaesthetist's point of view, for adequate payment of operating theatre technicians, and we are anxious that this issue should not be lost sight of in the midst of controversy on the desirability or otherwise of the employment of these men.

A letter from Mr. David Aiken in the *Journal* (April 14, p. 820) expresses the view of a surgeon that the modern operating theatre has no use for the services of technicians. This as a personal view is quite in order, but surely, Sir, in 1951, it is generally agreed that such men perform a most useful function, receiving the support of the great majority of surgeons and anaesthetists. Your annotation of January 13 (p. 80) and the letter from the President of the Royal College of Surgeons (March 10, p. 525) are evidence of this. Furthermore, some of your readers may be interested to know that the *Annual Report of the Council of the Association of Anaesthetists of Great Britain and Ireland* for 1950 states that "their employment is particularly essential at the present time in view of the considerable shortage of nursing

staff, and a number of them are being lost as a result of their promotion to less important but higher paid posts." It is because of the unsatisfactory pay of the technicians that our original letter was written, and we would like to re-emphasize the urgent need for regularizing their position.—We are, etc.,

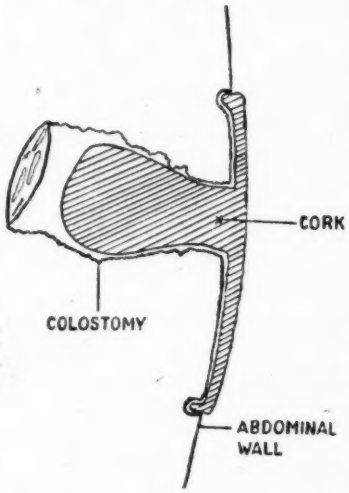
J. ALFRED LEE.
T. C. THORNE.

Westcliff-on-Sea.

Leaking Colostomy

SIR,—In an endeavour to help your correspondent in "Questions and Answers" (April 7, p. 772), a successful attempt of mine to solve this problem which had failed to respond to diet might be worth trying out.

An acrylic cork was constructed for a female patient and has now been worn with satisfactory results over the last three years, the cork being kept in position by her belt (roll-on). The technique of construction, which should come readily to a dental surgeon, is to take a composition impression of the first inch or so of the colostomy opening, and also including some 2 in. (5 cm.) of the adjacent abdominal wall, the muscles being in the relaxed position. To this impression a plastic cork is made, a small ¼-in. (0.6-cm.) lip being added around the periphery (see diagram). Care must be taken to clear the iliac crest and pubic bones, or the cork will dig in on sitting down. In the case I dealt with colic was encountered, which it was decided was due to attempts to expel the cork, and was avoided by narrowing the neck of the cork. The prosthesis is readily cleaned, hypochlorites being eminently suited for this purpose. On the question of retention, I have no doubt your correspondent will be able to devise some suitable elastic support.—I am, etc.,



JOHN HALLAM.

Liverpool.

Low Spinal Block in Eclampsia

SIR,—I wish to thank Dr. A. H. Galley (April 7, p. 762) for providing an explanation which fits in as a superstructure to the thesis I have advanced that resistance to stretch by the uterus provokes the Oxford shunt. A sufficiently large-scale glomerular shut-down of the Oxford pattern is associated with water and salt retention, largely a direct result of limited filtration. Renal ischaemia provides renal vaso-pressor substances—e.g., renin[1] and vaso-excitomotor substance (V.E.M.).[2] The latter is destroyed by the re-establishment of the renal blood flow.

Low level spinal anaesthesia by cutting off efferent stretch impulses from the uterus overcomes the Oxford shunt. It helps indirectly, therefore, in the destruction of the circulating V.E.M. also, and breaks the vicious circle hitherto operative. While severe shut-down in its early stages responds thus, later stages call for a direct attack on the renal innervation such as Hingson's caudal pavex technique.[3] The effectiveness of low spinal block emphasizes the aetiological importance of nervous impulses emanating from the uterus.

Tautness of the abdominal wall may enhance the efferent stimulus, which is chiefly uterine in origin. Intra-abdominal pressure rise is not, however, directly responsible for the renal change, which has the Oxford pattern and not that of simple compression. Goldblatt[4] advocated the slinging of the pre-eclamptic patient in the prone position, avoiding direct pressure on the abdominal wall, but this measure has been abandoned. Nevertheless Mr. R. H. Paramore's (March 31, p. 701) influence on obstetric thought will survive this generation, for he originated the non-toxaemic concept of the condition and emphasized the paramount importance of diminished urinary output as an indication of impending disaster.—I am, etc.,

JOHN SOPHIAN.

London, W.1.

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1 Goldblatt, H. (1948). *Amer. J. Med.*, **4**, 100.
2 Schorr, E. (1948) Ibid.. **4**, 121.
3 Hingson, R. (1948). Oral communication, Royal College of Obstetricians and Gynaecologists, June, 1948.
4 Goldblatt, H. (1948). Personal communication.

Paralysis after Anaesthesia

SIR,—It is sometimes difficult to make an anaesthetic mask fit a patient's face in an airtight fashion. Some years ago I described a simple device which usually solves this problem (H. J. V. Morton, 1944, *British Medical Journal*, **1**, 291). Recently I have been told of transient supra-orbital nerve paralysis due to its use. This complication is a pressure effect, which can be prevented by merely keeping the appliance clear of the patient's forehead. It is thus a complication unlikely to be encountered by those aware of its possibility.—I am, etc.,

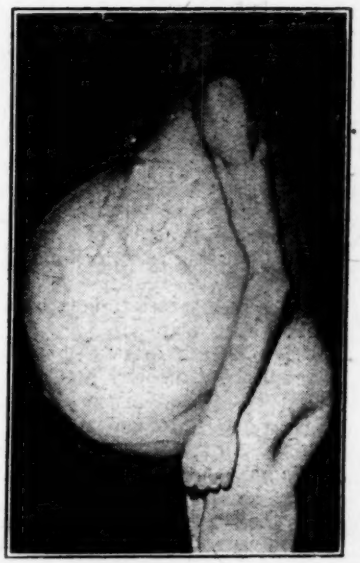
H. J. V. MORTON.

Hillingdon, Middlesex.

Enormous Ovarian Cyst

SIR,—The recording (March 24, p. 622) of an ovarian cyst of enormous size is almost certain to stimulate competition; nevertheless, in these days when the Old Country seems to be in danger of being outstripped by the world, I must record that England can hold her own with Ethiopia.

A woman aged 38 reluctantly consulted a woman doctor to obtain a free corset. The astonished doctor insisted on calling in her principal, in spite of his being male, and he asked me to pay a domiciliary visit. In this way we stumbled on a cyst even larger than that described by Professor R. J. Last. She was an emaciated woman more ashamed of her condition than frightened. The abdomen was uniformly distended, and a marked collateral network of veins was prominent everywhere. The skin was thick and oedematous. The girth was 54 in. (132.5 cm.).



She was admitted to hospital, and a few days later anaesthetized for operation. A midline incision was made and the cyst punctured. Thereafter basinful after basinful of thick brown fluid was borne away and measured till 57 pints (32.5 litres) had been collected. Then the cyst was with great difficulty removed, for it was adherent to the whole of the anterior abdominal wall above the umbilicus, but fortunately not to the viscera. As the operation proceeded a transfusion was commenced; two pints were transfused. Eventually the whole cyst, containing one more medium and innumerable small loculi, was removed. The abdomen then presented the same curious appearance as that described by Professor Last. The thorax had been splayed upwards so that on picking up the skin at the end of the wound one peered into a vast Gothic cave on the floor of which were the thin, flattened, devitalized viscera tracing out a grotesque mosaic. She was severely shocked and her pulse was uncountable, but she responded well to methedrine (30 mg. intravenously, repeated in four hours intramuscularly) and to further transfusion of blood (one pint) and of plasma (two pints). Convalescence was uneventful. She was up on the third day, and discharged

home on the fourteenth, since when she has flourished and progressed in a satisfactory manner.

It is unfortunate that the patient's weight before and after operation was not recorded, but with 57 pints measured, some spilt, and some left behind in the smaller loculi, it is probable that the tumour weighed as much as the patient. The surprising thing is that she had carried it about and done her household duties for at least two years.

Professor Last has acknowledged his debt to Lister. I must also record what we owe to the State for providing corsets, to modern anaesthesia, and to the anonymous legion of blood donors without whom this woman would not have survived a one-stage operation.—I am, etc.,

Blackheath, S.E.3. KEITH VARTAN.

Identity of Hookworm in the Throat

SIR,—I reported (November 18, 1950, p. 1173) a case of worms found in the throat of a girl in St. Lucia. I have received a letter from Professor R. T. Leiper, of the Commonwealth Bureau of Agricultural Parasitology, raising the question of the worms being *Syngamus kingi* and not, as I reported, *Necator americanus*.

A somewhat similar case occurred in St. Lucia many years ago. The worms were sent by Dr. King to Professor Leiper for identification, and the latter published a report on them (*Trans. R. Soc. trop. Med. Hyg.*, 1913, **6**, 265). Professor Leiper identified the worms as Syngamus, and named them *Syngamus kingi*. At the time of writing my previous letter I was not aware of Professor Leiper's report, and unfortunately my specimens were not preserved, so that I was unable to re-examine them in the light of this new knowledge.—I am, etc.,

St. Lucia, British West Indies. A. V. WELLS.

New Operation for Peptic Ulcer

SIR,—In 1931 Ivy stated that he was about to give up his experimental work on peptic ulcer as he was unable to produce in animal experiments conditions of pylorospasm and reflex nervous disturbance in a dog as they are known to occur in man. It is therefore apparent that the principles elucidated by experimental research can be applied to the human subject only with considerable reserve.

It is true that in McCann's dogs 80% developed ulcers within three months of operation, but at post-mortem examination the presence of ingested hair and gross food particles embedded in the ulcer suggested a mechanical origin to the ulceration. In his summary McCann is at pains to state: "Evidence was obtained which substantiated Mann's interpretation of the important mechanical factors that are active in causing these experimental ulcers and of the destructive friction of coarse cellular foods on the reparative granulation and epithelial cells of a healing ulcer." Such severe trauma by ingested foods is surely not applicable to man.

It is only fair to state that the high incidence of peptic ulceration obtained by McCann has not been experienced by all workers. Wangensteen writes, "We, too, have eight dogs with the McCann application of the Schmilinsky procedure. All appear well. Four have been re-explored after the lapse of at least four months, but no ulcers have been observed."

Ivy and Fauley carried out the operation in 12 dogs, two of which died of distemper. Of the remaining 10, two only developed ulcer. Of four dogs used as a control group, in which the pylorus was simply cut across and resutured, one developed a duodenal ulcer, so that the development of ulceration in the two dogs on which the procedure was performed may well be due to operative factors not applicable in the human subject. A continuation of their experiments consisted in re-operating on their eight ulcer-free dogs, freeing the jejunal loop anastomosed to the stomach and reimplanting it into the distal small intestine. Seven of the dogs developed ulcer and the eighth died of inanition. In spite of McCann's claim that a shunt operation has no effect on the acidity of the chyme, these experiments of Ivy and Fauley surely suggest that the presence of the total duodenal secretions in the stomach prevented the incidence of ulceration in seven out of their eight dogs.

In the human patient our post-operative studies of gastric acidity have not corresponded to McCann's experimental work and there has been reduction to achlorhydria or normal limits.

In Finney's pyloroplasty it is unlikely that these duodenal secretions regurgitate into the stomach in quantity, as active peristalsis would seem to be sufficient to prevent this, and in a low gastrectomy the rapid emptying rate of the viscus as revealed by a post-operative barium meal suggests that free admixture of stomach and duodenal content does not take place in that organ.

The operation of Schmilinsky bears little resemblance to that described in my article, as readers of his original paper will observe. It is therefore of little value to quote the severe post-operative complications associated with it and to infer that they will occur necessarily following my suggested procedure.

The cases I originally reported (March 3, p. 454) remain fit and well. Their numbers are now nearly trebled, and there is no suggestion of recurrent ulceration. The final assay of this operation must wait, but it would be wrong to judge it by McCann's observations. Were these applicable I should now be dealing with well over 20 recurrent ulcers, but instead I have more than that number of well-contented patients. I hope that this letter will answer the friendly criticisms of your correspondents in your issue of April 14, page 817.—I am, etc.,

London, W.1. STANLEY O. AYLETT.

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Ruptured Tendon after Colles's Fracture

SIR,—In your issue of April 7 (p. 751) there appeared an article by Mr. H. Osmond-Clarke as part of a refresher course for general practitioners; it was surprising to read in dealing with rupture of the extensor longus pollicis tendon, as it occasionally occurs after a Colles's fracture, that the tendon is "gradually frayed through by constant friction on the irregular fracture line." Examination of the anatomy of the ruptured tendon does not support this view: as Mr. H. Osmond-Clarke favours tendon transplantation rather than the easy operation of direct suture of the ruptured tendon his experience of the immediate local condition is probably limited, and accounts for his repetition of the time-honoured but inaccurate statement of the frayed tendon.

In a series of 12 personal cases where the local anatomy has been carefully studied it was found that the groove on the dorsum of the lower end of the radius was even, with no sign of any irregularity. The ruptured ends of the tendon, far from presenting the appearance of fraying, were swollen, rounded, yellowish with streaks of bruising but perfectly smooth; connecting each end was a long, thin, smooth strip of tendon attenuated like a drawn-out piece of chewed chewing-gum; the tendon substance must have undergone considerable softening for this to occur.

The available evidence points to the cause of the spontaneous rupture as the result of aseptic avascular necrosis of the tendon, due to damage to the blood supply at the time of the injury with subsequent softening and elongation of the tendon. This was suggested by Weigeldt and later by Hauck; the facts support this contention rather than the inaccurate statement of "fraying through by constant friction on the irregular fracture line."—I am, etc.,

London, W.1. DAVID TREVOR.

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Tuberculosis in Kenya

SIR,—In his article (January 13, p. 67) Dr. W. S. Haynes credits me with making a sweeping and ridiculous assertion and then states that all subsequent work contradicts this assertion. I have never stated that the African never recovers from his primary tuberculous infection; on the contrary, in the article to which he refers I several times mentioned the finding of healed primary tuberculous complexes in Africans at necropsy (Davies, J. N. P., *E. Afr. med. J.*, 1947, **24**, 352). What I did state was that, based on 3,000 necropsies, "while there is evidence that a few cases may heal a primary complex there is no case of anything other than a primary complex being healed. It would appear that the vast majority of cases of tuberculosis in Uganda are those which have failed to overcome their primary infection." Stott (1950) appears to have the same situation in his cases in Nakuru prison.

Dr. Haynes appears to think that pathologists in East Africa base their opinions on tuberculosis solely on the study of patients dying of tuberculosis. This is quite incorrect; tuberculous patients form only a small proportion of the cases coming to necropsy at this hospital. In those who do not die of tuberculosis, tuberculous lesions, chronic phthisis, unsuspected tuberculosis, and healed phthisis are extremely rarely seen, and, though a few healed primary complexes are seen, they are not frequently met with and not in proportion to the high incidence of positive tuberculin reactors in the community at large. This contrasts with experiences elsewhere (Todd, 1927; Carnes, 1942). When this article was written the likelihood of such a high incidence of tuberculin reactors in adults in Uganda was suspected from the work of Connolly (1941) in the adjacent Nyanza province of Kenya, and this has now been confirmed for Uganda. But if there are many cases of chronic tuberculosis perambulating about Uganda, as Haynes supposes is the case in Kenya, why are they so rarely seen clinically or at necropsy? How is it that they do not die of accidents, of other infections, or of surgical conditions?

The situation at Mulago Hospital is apparently similar to that met with by Stott at Nakuru. Either, broadly speaking, an African shows no evidence of tuberculous infection (other than perhaps a positive tuberculin test) or he is extremely ill and dies with a fulminating type of the disease with glandular involvement, and in many cases with evidence of direct progression of the disease from a Ghon focus.

Dr. Haynes's whole argument is based on his assumption that a positive tuberculin test has the same significance, at the same level of sensitivity, in Africans as in Europeans. He did attempt to exclude false positive reactions due to leprosy. But there are other acid-fast bacilli to be considered, such as those causing skin ulceration described by MacCallum (1948), or those which cause skin lesions with false positive tuberculin reactions in cattle (Daines, 1938). There is the possible effect of malaria on the tuberculin reaction, to which Makari (1947) drew attention. These are only a few of the points that should be considered in discussing tuberculosis in East Africa. Work is in progress at this hospital which will, it is hoped, advance our knowledge further and answer some of these questions. I consider that much further work is needed in East Africa before we can begin to tackle this very important disease, and until it is done there is little profit in discussion. The purpose of this letter is not to initiate such discussion but to protest against a flagrant misrepresentation of my views.—I am, etc.,

Kampala, Uganda. J. N. P. DAVIES.

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Free Burial

SIR,—During the last year we have had four cases of distress caused by the death of a person whose relatives were unable to meet the expenses of burial. As doubtless you know, provision was made under the National Assistance Act of 1948 to meet such cases, but we find that there are many who are not aware that local authorities will provide free burial.

I have discussed this matter with the local burial superintendent and also with my bureau committee, and we think that doctors may care to give this information to relations, when making out the burial certificate, where it seems there may be difficulty in finding the funeral expenses.—I am, etc.,

Citizens' Advice Bureau, Sussex. R. FORDE.

POINTS FROM LETTERS

Megaloblastic Anaemia and Syphilis

Dr. P. H. BIRKS (Doom Dooma, Upper Assam) writes: The article by Henry Foy, Athena Kondi, and A. Hargreaves on the treatment of a case of megaloblastic anaemia with penicillin (February 24, p. 380) stimulated the imagination. I was disappointed to find no mention of a Kahn test. This surely nullifies the whole article. In Assam it is not uncommon to find syphilis a major stress factor in megaloblastic anaemia.

Sharp Edges and Boiling

Mr. JOHN FOSTER (Leeds) writes: . . . Physical injury to sharp-edged instruments by boiling is unquestionable. Naturally the effect of this is of very much more account in ophthalmic surgery than in general surgery. See my papers in *Proc. R. Soc. Med.*, 1946, **39**, 460, 835.

Mitosis Prevented by Waste Products

Dr. R. L. WORRALL (Sevenoaks, Kent) writes: Your otherwise comprehensive leading article on mitosis (April 14, p. 803) omits the significance of waste products as inhibitors of cell division. If a living cell is considered as a steady state system, in dynamic equilibrium with its environment, all its activities are seen to depend upon a sufficiently free exit of waterborne waste products, particularly carbon dioxide and nitrogenous compounds. . . . The importance of carbon dioxide in this respect is evident, for if the carbon dioxide concentration in a growing (bacterial) culture is sufficiently increased, with the gas under slight pressure, cell multiplication is inhibited to an extent varying with the organism concerned. Tissue culture of mammalian cells also indicates the validity of the above conclusion, that the mutual proximity of cells tend to check their growth by more or less flattening out the local concentration gradients of waste products around each cell, thus reducing the diffusion rates of the waste products away from the cell surface. Tissue culture cells only multiply when they have migrated outwards from the periphery of the culture and have thus become sufficiently separated from one another. . . . Elsewhere I have put forward the view that the autonomy of cancer cell growth is due to the heritable resistance of cancer cells to carbon dioxide concentrations which limit the growth of normal cells.

Chlorophyll as a Deodorant

Dr. ANNA M. HERDMAN (Edinburgh) writes: With reference to a question asked on this subject (April 7, p. 772), a recent case may be of interest. My patient, a woman aged 72 years, was suffering from advanced carcinoma of the pharynx. Her breath was so offensive that the nurses were nauseated when attending to her. I prescribed tablets of chlorophyll and yeast, two thrice daily. After the second day of taking these tablets the disgusting odour went completely, and did not return as long as they were given regularly.

Early Expert Witnesses

Mr. L. A. PARRY (Hove) writes: . . . Sir Sydney Smith mentions (March 24, p. 599) some famous medico-legal cases of old times. I should like to add one to this list, as it is the first case I have been able to trace of murder by poison in which medical witnesses were called to prove the cause of death. It is that of Mary Blandy, tried at Oxford in 1752 for poisoning her father with white arsenic. Dr. Anthony Addington and other medical practitioners gave evidence for the prosecution, but their testimony related to the clinical symptoms and the pathological findings, and no attempt was made to analyse the viscera, though many tests were known for the detection of arsenic and were actually employed in this case to determine the nature of the powder administered to the deceased. She was found guilty.

Obituary

J. GAY FRENCH, M.S., F.R.C.S.

Mr. J. Gay French, consulting surgeon to the Ear, Nose, and Throat Department of the Royal Free Hospital, died in London after a short illness on April 13, in his 80th year.

John Gay French, whose father was Lieutenant-Colonel J. Gay French, of the Indian Medical Service, was born in India. He was educated privately and studied medicine first at Trinity College, Dublin, and later at St. Mary's Hospital, London, to which he obtained an open entrance science scholarship. Qualifying in 1902, he immediately started on his study and practice of the diseases of the ear, nose, and throat, which led him finally to the charge of departments at the Royal Free Hospital and the Royal Masonic Hospital. After resident appointments at St. Mary's, St. Bartholomew's, Great Ormond Street, and Golden Square, he was elected to the staff of the Royal Northern Hospital in 1906 and the Central London Throat and Ear Hospital in 1907. In that year he became a Fellow of the Royal College of Surgeons of England, and also took the M.S., London. He joined the staff of the Royal Free Hospital in June, 1911, eventually becoming senior surgeon in the ear, nose, and throat department and also a lecturer in the medical school. During the first world war he was a consultant to the War Office, and in later years he was an examiner in laryngology and otology to the Royal College of Physicians and Surgeons. He made many contributions to the literature of his specialty.

J. D. McL. writes: In Gay French's early years of hospital work specialists in ear, nose, and throat surgery were still fighting for recognition, and by his skill and personality he contributed a large part to the successful issue of that battle. Temperamentally he was not capable of working at half speed. His department was run autocratically, and every detail received his personal attention, while his abounding energy overflowed to the control of the administration of the Royal Free Hospital as a whole. For many years he acted as chairman of the medical committee, and there his authoritative decisions received the respect which his obvious sincerity and singleness of aim deserved. He taught with fervour and with a shrewdly common-sense outlook, so that his clinics were as much a lesson in the art of dealing with patients as in the science of medicine. His students loved him, for, however fierce his front, their interests were patently his concern. The same quick human sympathy bound his patients to him. He was to them the true physician, to whom the individual was more important than the disease. He had no bleak scientific concentration on pathology, but his kindly interest encompassed not only the sick but their friends and relations and all their human contacts. With these qualities he was bound to amass a large private practice, and for many years there can have been few busier surgeons. The Royal Free Hospital paid him the great compliment of twice extending his tenure of office after the normal retiring age had been reached. When the inevitable parting came, it was with regret on both sides. Fortunately, many years of active medical life remained to him; he could never have vegetated in complete retirement. The last years of his life were clouded by personal loss and bereavement in a family to whom he was passionately attached, and our great sympathy must go to Mrs. Gay French, who remains to mourn with us his passing. He was a great character.

F. K. KLEINE, M.D.

Dr. F. K. Kleine, whose death at the age of 81 is announced from Johannesburg, was for many years a notable figure in tropical medicine.

Friedrich Karl Kleine was born in Stralsund in 1869, the son of a doctor, and studied medicine at Halle University, qualifying in 1895. He first joined the medical corps of the German Army, but at an early stage he developed a keen interest in bacteriology, and in 1900 he joined Robert Koch, who was in charge of the Institute for Infectious Diseases in Berlin. In 1903 with Koch he went to Rhodesia, where they studied the transmission of East Coast fever in cattle by ticks. A few years later he took up the study of tick fever in dogs, and in 1906 he again visited East Africa with Koch as a member of the German sleeping sickness expedition. Henceforward trypanosomiasis in man and animals became his chief interest. In 1908 he proved that trypanosomes undergo a cyclical development in tsetse flies and that transmission is not purely mechanical. This observation was of great importance for the fuller understanding of the epidemiology and control of trypanosomiasis. After the first world war Kleine was one of the first to investigate the possibilities in trypanosomiasis of antrypol, or Bayer 205 as it was first called. In connexion with the study of this compound, which after 30 years still retains its importance, he visited Northern Rhodesia and the Belgian Congo in 1921, describing his investigations to the Royal Society of Tropical Medicine in 1923. It was very largely owing to Kleine's work that antrypol was made available for the treatment of trypanosomiasis in cattle, and, with Fischer, he was one of the first to point out the possibilities of chemoprophylaxis. In 1926 Kleine was again in Central Africa as the German member of the League of Nations Sleeping Sickness Commission. Here he became greatly interested in the question of immunity to trypanosomiasis in man and animals, a subject on which he continued to do much work, for he was convinced that immunity was acquired and could undoubtedly be produced artificially. Subsequently he became director of the Robert Koch Institute in Berlin, but the subjects which interested him—relapsing fever, rinderpest, and foot-and-mouth disease in the Tropics—gave him many opportunities for returning to Africa. In 1947 he finally settled in Johannesburg, where he enjoyed a few years of happy retirement in the company of his wife, who before her marriage in 1921 had been Miss Hanne Ockelmann, an assistant at the Robert Koch Institute.

Kleine belied his name, for physically and mentally he was in his heyday a big man with big ideas. He maintained the best traditions of the German scientist, and all his expeditions to Africa were carefully planned and well equipped. Some of the equipment which he and Koch took out to Tanganyika was in fact still serviceable during the war years in the pathological laboratory at Dar-es-Salaam. His long association with Koch is a reminder of the rapidity with which bacteriology has developed as a science. Kleine had many difficulties

to contend with in the furtherance of his investigations, but his sense of humour, loyalty, and never-failing courtesy endeared him to many friends in many countries.—G. M. F.

Although he had been in practice for only three and a half years, a wide circle of patients and friends learned with regret of the death of Dr. J. M. G. SARSON in University College Hospital on March 10. The eldest son of Canon and Mrs. Sarson, now of Woodbridge but for many years resident in Chester, John Malcolm George Sarson was educated at Rishworth School, Halifax, and graduated M.B., Ch.B. at Liverpool University in 1942. After holding the post of senior casualty officer at the Liverpool Royal Infirmary he joined the R.A.F. After demobilization he went into practice in Wembley, first as assistant and then as a partner. Here he was rapidly making a place for himself in the life of the district. He participated fully in the general-practitioner activities of the local hospital, which he much valued, was elected assistant secretary of the newly formed Wembley Division of the B.M.A., and found himself at home in Church and "round table" circles, where his social gifts and interests were fully employed. John Sarson married while in the R.A.F., and leaves a wife and four young children. He was only 34, but general practice is the poorer for the loss of a practitioner of ability and of the utmost integrity, who was aware of and would have maintained its best traditions.—H. M. H.

Dr. HARRY MARTINDALE SPEECHLY, a provincial coroner in Manitoba for 22 years, died at Winnipeg on March 17, aged 84. He went to school in Cambridge and Bath, and studied medicine at the London Hospital, qualifying in 1889. He practised at Parkgate, near Birkenhead, from 1893 to 1901, and then went to Canada. From 1901 to 1916 he was a general practitioner in Pilot Mound, Manitoba, returning to England to serve in the R.A.M.C. as medical officer to Fleet V.A.D. Hospital during the first world war. In 1919 he went to Winnipeg, where he lived until his death. Besides being coroner, he was lecturer in forensic medicine to the University of Manitoba. In 1943 the University of Manchester conferred on him the honorary degree of LL.D. He is survived by his widow, two sons, and a daughter.

R. M. writes: The death of Dr. H. M. Speechly removes a link with a bygone age, that comfortable unhurried world before the first world war. Something of the serenity of that period clung to him and communicated itself to others. Throughout his life he carried the idea of service, and each community in which he lived was the richer for his presence. He was a many-sided man. As a physician, well-trained and well-read, he served faithfully, but other interests, notably natural history and the Anglican Church, were equally dear. His medical life began in 1884, when, at 18, he entered the London Hospital medical school. At that time the clinical thermometer, a foot long, was still looked upon as a scientific toy. He was clerk to Hughlings Jackson and listened eagerly to Frederick Treves on surgery. Wilfred Grenfell, of Labrador, was a classmate. Speechly's connexion with India, where he was born and where his father was the first missionary bishop of Travancore and Cochin, made him conscious of the ravages wrought by malaria. Sir Ronald Ross became his medical hero. Speechly's knowledge of the life history of the mosquito led him in later life to take up with characteristic energy mosquito control in Greater Winnipeg. In this he was spectacularly successful, and he became an authority on the subject. During his years at Pilot Mound, 1901 to 1916, he was keenly interested in the flowers and fruits of his prairie garden, and he was always ready to pass on to others his knowledge. Like Bacon, he considered the planting of a garden as the rarest of human pleasures. He never faltered in working for the Anglican Church. At his death he was the oldest lay reader in the diocese, and he was a frequent delegate to synod meetings. When the British Medical Association met at Winnipeg in 1930 he organized in connexion with the religious service a procession and pageant which was a most impressive spectacle. He served in both world wars: during the first he was in England, and during the second he was assistant medical officer at King Edward Hospital, Winnipeg. The Canadian Medical Association named him as a senior member in 1941. No mention of his life would be complete without reference to his wife, who was a true helpmeet.

Dr. J. H. GIBSON, who was for over 60 years a general practitioner in Aldershot, died at his home in that town on March 20, aged 92. The son of a farmer, John Hutchinson Gibson was born at Bassingthorpe, Lincolnshire, and was educated at King's School, Grantham, and Guy's Hospital, London, qualifying in 1882. In 1886 he went into partnership in Aldershot, where he remained for the rest of his life. Gibson played an important part in establishing the Aldershot Hospital; he was senior physician on the staff and chairman of the medical council for some years before retiring from practice in 1948. He held the appointments of medical officer to the Farnham Guardians for many years and afterwards to the Hants Public Assistance Committee. He had been a member of the B.M.A. since 1887. A keen archaeologist, Dr. Gibson was a member of the Royal Archaeological Institute of Great Britain, the Surrey Archaeological Society, and the Hampshire Field Club, often contributing articles to the journals of these societies.

Dr. MALCOLM DONALD MACAFFER died in Glasgow on April 1 at the age of 37. He studied medicine at Glasgow University, graduating M.B., Ch.B. in 1943. He then spent six months as a house-surgeon at the Royal Infirmary, Glasgow, before joining the R.A.M.C., in which he served for three years, attaining the rank of captain in 1944. After demobilization he took the post of house-surgeon at the Maternity Hospital, Bellshill, where he remained for a year before spending six months in the same capacity at the Royal Samaritan Hospital, Glasgow. In 1948 he returned to his native town as an assistant in general practice. Invariably cheerful and kindly, his untimely death caused the loss of a young doctor very popular among his colleagues.—N. D.

Cheltenham and the surrounding countryside suffered a severe loss by the sudden death of Mr. J. S. ROBINSON at the age of 64 on April 1. James Salmond Robinson was the son of Mr. Andrew Robinson, C.B.E., M.V.O., of Belfast, and was born in Dublin. He graduated M.B., B.Ch. at Trinity College in 1915, and after holding resident appointments in Dublin he joined the R.A.M.C. and served in India from 1915 to 1918. He came to Cheltenham as house-surgeon in 1919, and went from there to Birmingham to take a special course in orthopaedics. In 1922 a new department of orthopaedics was opened at the Cheltenham General Hospital by Sir Robert Jones, and Robinson was put in charge. This orthopaedic centre, the first of its kind in Gloucestershire, grew rapidly, and Robinson was appointed orthopaedic surgeon to the county. In addition to his orthopaedic work he was a brilliant general surgeon and became consulting surgeon to Cheltenham College, Cheltenham Ladies' College, Dean Close School, and to the hospitals at Fairford, Winchcombe, Tewkesbury, Cirencester, Evesham, and Bourton. He was president of the Gloucestershire Branch of the B.M.A. from 1938 to 1946, and only a few weeks ago he gave an instructive address to the Branch on "Diseases of the Knee-joint." In the summer of 1945 he had a serious illness which necessitated a major operation, but, undaunted, he made a good recovery and was soon back at work.

J. R. C. writes: As a general surgeon Robinson was often needed in an emergency, and no appeal from a colleague for his help was ever refused. No matter how tired he might be or how untimely the hour, Robinson turned out, ever his cheerful self. I think his outstanding characteristic was his goodness of nature. He saw the best in everyone,

and in consequence was able to draw out the best from those among whom he moved. All felt that they could rely on his straightness, calm judgment, and skill. In his time doctors were judged by two juries—the general practitioner by the jury of his patients and the consultant by that of his fellow practitioners. There are now other modes of assessment. Robinson won the warm approval of all by his personality and professional attainments. The esteem in which he was held was shown by the crowded congregation at the funeral service held at Charlton Kings church. The church was filled to overflowing; many doctors from Cheltenham and distant parts of the county attended to show their respect for one whom they loved and who had brought honour to their profession. A memorial service was held in Cheltenham College chapel on April 7. Much sympathy will be felt with his wife, who upheld him always, and with his son and daughter.

Dr. FRANK ERNEST ANDERSON, who died at his home in Bungay, Suffolk, on April 13 at the age of 51, received his medical education at St. Andrew's University, where he graduated M.B., Ch.B. in 1922. After holding appointments as gynaecological and surgical house-officer at Dundee Royal Infirmary, he joined the Sudan Medical Service, and was posted to various stations in that country, being finally appointed senior medical officer in charge of Port Sudan and the Red Sea province. Here he did excellent work, particularly in connexion with the Mecca pilgrimage quarantine and among the Hadendoa tribe of the Red Sea hills. In his spare time he kept open house, and a visit to Dr. and Mrs. Anderson became an institution with British officials going on leave and coming from it. The responsibilities of a growing family brought him back to England in 1935, and he settled in partnership in Bungay. Here he was just finding his feet, when the outbreak of war led him to volunteer for the Territorial Army. He was sent to Singapore as major with a field ambulance attached to the ill-fated 18th Division, which arrived there shortly before the capitulation. He served as medical officer to various prison camps on the island, and his devoted work among his fellow prisoners earned him a mention in dispatches, and will be long remembered with gratitude by many Norfolk men. Unfortunately, his own health suffered severely, and he returned to England a sick man, finally contracting a fatal malady as a result of his war service. In spite of this, and the tragically sudden death of his wife 18 months ago, he kept resolutely at work in his practice until within a few months of his death, bearing his increasing disability with a cheerful fortitude which was the admiration of his colleagues. He leaves a son and a daughter.—C. G. H.

Medico-Legal

DEATH AFTER ANAESTHETIC AT CIRCUMCISION OPERATION

[FROM OUR MEDICO-LEGAL CORRESPONDENT]

Whatever may be the merits of circumcision, a subject discussed in this *Journal* just over a year ago,[1] the risks inherent in administering anaesthetics to very young children are illustrated by a recent tragedy in Yorkshire. On advice received at the Halifax General Hospital, Mr. and Mrs. Arthur Jowett, of Halifax, decided to have their son Michael, aged 5½ months, circumcised. On the day before that fixed for the operation Michael had a cold and cough, and his mother took him to see their family doctor. Next day at 10 a.m. she took him to the Halifax General Hospital. She told the sister with whom she left him that he had a cold and cough. When she collected him at 3 p.m. that afternoon he seemed to be listless, and on the following day she noticed that his breathing was wheezy. On the second day after the operation he seemed to be so ill that Mrs. Jowett again called in her doctor. Michael was taken back to hospital by ambulance, and there, in spite of being given oxygen, penicillin, and stimulants, he died early next morning, two and a half days after the administration of the anaesthetic.

At the inquest held before the Halifax Borough Coroner on March 21 evidence was given by the resident anaesthetist at the hospital, who had given the anaesthetic. He had used atropine 1/200 gr. (0.32 mg.) as premedication. This was followed by inhalation of open ether in the dorsal decubitus position, and administration had lasted 10 to 12 minutes. He had found the child a normal healthy-looking infant. He had not made a detailed examination of him before giving the anaesthetic, nor had he taken his temperature, examined his lungs, or sounded his heart. It was usual to examine the chest before giving an anaesthetic. So far as he knew no one else had made a detailed examination of the child. It was his responsibility as the anaesthetist to see that the child was fit to have an anaesthetic. He said that if he was satisfied that the lungs were not involved, the fact that a child had a cold or cough would not prevent him from giving it an anaesthetic, though to do so would be dangerous if it was suffering from bronchopneumonia. If he knew a child had a severe cold it might deter him from giving it an anaesthetic.

Dr. H. V. Phelon, pathologist at the Royal Halifax Infirmary, who made the post-mortem examination, said the lungs showed widespread patches of bronchopneumonic consolidation, and gave his opinion that death was caused by bronchopneumonia. Dr. Phelon said that before a child was given an anaesthetic it should have its temperature taken and its heart and lungs tested. The administration of ether to a child with a cough and cold would increase the risk of infection of the upper respiratory tract. The administration of ether was, in his opinion, associated with the bronchopneumonia which had caused the death.

The verdict was recorded of death by misadventure.

[1] *British Medical Journal*, 1949, 2, 1433, and subsequent correspondence.

Medical Notes in Parliament

Care of the Aged

In moving the motion in the House of Lords on April 18 calling on the Government to ensure that adequate attention and service are available for old people, Lord SALTOUN said that last year he had been unable to obtain either facts or figures on the subject from the Government, and had therefore been forced to collect his own. Over the space of six months 17 people had been found dead in varying conditions of horror. So far as he could see the difficulty was that such people were the responsibility of no one in particular, not coming under the jurisdiction of either the Ministry of Labour, the National Assistance Board, or the Ministry of Health. Hospitals were intended to heal the sick, and not to serve as homes for chronic and incurable cases. Some had managed to open chronic wards, but not enough, and they were often "landed" with old people when the relatives did not take them back.

HOSPITALS REFUSE ADMISSION

Frequently, hospitals refused to admit an old patient; doctors had been known to threaten to refuse to sign a death certificate. In six months 11 hospitals had refused such cases. Neither the National Assistance Board nor any other authority paid the cost of maintaining patients in private nursing-homes or hostels, though in certain cases they did pay part. Lord Saltoun maintained that it was essential to have an officer with adequate powers to know and deal with all cases in his especial district. Lord KERSHAW denied that the absence of a relieving officer of the type known under the old Poor Law system was the real reason for the

cases quoted. He agreed that the most constructive suggestion put forward was that there should be better co-ordination between the Government departments concerned. He referred to an interesting experiment at present being made in some areas which provided specialist services at the homes of the chronic sick. The various departments of public administration were very alive to the necessity of development.

Lord AMULREE said that some chronic sick hospitals had waiting-lists up to 12 months. He pointed out that prompt admission should normally ensure quick discharge, and considered that proper use of available beds should be encouraged.

HALF-WAY HOUSES

THE ARCHBISHOP OF YORK referred to the problem of those who were not ill enough to go to hospital yet not well enough to look after themselves. He considered that half-way houses should be places where old people could go, and have a certain amount of supervision, possibly for the rest of their lives.

Lord SHEPHERD thanked Lord Saltoun for raising the subject and the motion was agreed to.

Admission of Chronic Sick

Miss I. WARD asked on April 19 whether the Minister of Health would make it a statutory obligation on regional hospital boards to accept cases recommended by medical officers of health as needing care and attention. Mr. H. MARQUAND replied "No."

Risk of Smallpox

Asked by Mr. THOMAS REID on April 5 what precautions had been taken to prevent the influx of smallpox from Calcutta, where deaths from this disease exceeded 500 a week, Mr. A. BLENKINSOP said that special care was being taken by airport medical officers, and travellers by air were given a warning notice. Travellers by sea passed out of the incubation period for smallpox before they arrived in Britain.

Colonial Medical Service

Mr. JAMES JOHNSON asked on April 11 how many hospitals and dispensaries had been closed down in Kenya and Sierra Leone through shortage of doctors, what steps were being taken to recruit African doctors in Great Britain for the Colonial Medical Service, and how many scholarships for medical training had been awarded during the last three years by the Governments of Kenya and Sierra Leone.

Mr. JAMES GRIFFITHS answered that no hospitals or dispensaries have been closed in Kenya. In February, 1951, staff shortages made it necessary temporarily to close two hospitals in Sierra Leone. Posts in the Colonial Medical Service were widely advertised, and African medical students were encouraged to apply for them. During the last three years the Kenya Government awarded 17 scholarships for medical training and also paid £21,000 to Makerere College for the training of African medical officers. The Sierra Leone Government had made seven awards, and two awards had been made to Sierra Leone students from the Central Allocation of Colonial Development and Welfare Funds.

Mentally Defective Children

In answer to a question on April 12 Mr. H. MARQUAND said that the need for more homes and institutions for mentally defective children was urgent, and the attention of regional boards had been drawn to the matter, since provision of accommodation was their responsibility. Because of the need for more nursing staff for these homes, nurses were being recruited from France.

Morphine on the Railway

Commander J. F. W. MAITLAND asked the Minister of Transport on April 16 whether he would include morphine in the first-aid equipment carried on trains. Mr. A. J. BARNES replied that the risks of the misuse of this dangerous drug would outweigh any possible advantages. Doctors carrying morphine and other drugs were almost invariably on the scene of the accident quickly.

Dentures and Spectacles

On April 17 the National Health Service Bill was presented, authorizing charges for certain dental and optical appliances and making provision for the accommodation and treatment abroad of those suffering from respiratory tuberculosis. The charge proposed for a full set of dentures is £4 5s., and for a pair of glasses 20s., plus the cost of the frames, which ranges from 3s. 4d. to 15s. 1d. The total cost for tuberculosis patients is estimated to be "not more than £200,000."

In answer to a question from Commander A. H. P. NOBLE the Minister of Health stated that had these charges been made from the start of the National Health Service £50m. would have been saved.

Tuberculosis in Foreign Workers

On April 19 Mr. W. J. TAYLOR raised the matter of the prevalence of pulmonary tuberculosis among foreign workers in Bradford, pointing out that of 225 European volunteer workers examined in Bradford 52 were found to be tuberculous and a further 21 suspect. He asked whether there should not be a much stricter medical examination on entry into this country.

Mr. H. MARQUAND replied that in the years 1947–50 there were respectively 0, 6, 15, and 26 infections of respiratory tuberculosis among foreign workers in Bradford, representing 2.29%, 5.4%, and 10.4% of the total notified infections in that city. He was examining whether more could be done to prevent immigration of foreign workers with tuberculosis.

Cope Committee's Reports

On April 19 Mr. H. MARQUAND stated that the recommendations made in the majority reports for the registration of medical auxiliaries would require legislation, and discussions were accordingly now being started with the various organizations concerned. Meanwhile it was intended to apply the recommended qualifications to new applicants for posts in the National Health Service.

Drunkenness in London.—Convictions in the Metropolitan Police District for drunkenness during 1950 were 16,760. The comparable figure for 1946 was 9,107. The same trend prevails all over the country.

Tuberculosis.—On December 31, 1950, the number of persons in England and Wales suffering from tuberculosis and waiting to enter sanatoria was estimated to be 10,400.

Slimming by Television.—The B.B.C. did not ask the scientific officers of the Ministry of Food for any advice on the slimming diets recommended to the public by television.

Travelling Expenses of Patients.—These are paid by hospitals only where hardship would otherwise be caused, and the need is determined in each case by the National Assistance Board.

Chronic Sick.—On December 31, 1950, there were 1,324 patients awaiting admission to chronic sick beds in the county of London.

Hospital Registrars.—Discussions are still proceeding on their future.

Hearing-aids.—It is not yet known when bone-conduction hearing-aids will be available in sufficient numbers to meet the known need.

Release from Broadmoor.—In the 10 years up to the end of 1950, 148 men and 61 women have been discharged from Broadmoor Institution.

Medicine Bottles.—The Minister of Health does not intend, in spite of the shortage of medicine bottles, to make a small charge to ensure their return.

INFECTIOUS DISEASES AND VITAL STATISTICS

We print below a summary of Infectious Diseases and Vital Statistics in the British Isles for the week ending April 7 (No. 14).

Figures of notified *cases* are for: (*a*) England and Wales (London included). (*b*) London (administrative county). (*c*) Scotland. (*d*) Northern Ireland. (*e*) Eire. Figures of *births and deaths* and of *deaths* recorded under each disease are for: (*a*) The 126 great towns in England and Wales (London included). (*b*) London (administrative county). (*c*) The 16 principal towns in Scotland. (*d*) The 10 principal towns in Northern Ireland. (*e*) The 13 principal towns in Eire. A dash — denotes no cases; a blank space denotes disease not notifiable or no return available.

The table is based on information supplied by the Registrars-General of England and Wales, Scotland, Northern Ireland, and Eire, the Ministry of Health and Local Government of Northern Ireland, and the Department of Health of Eire.

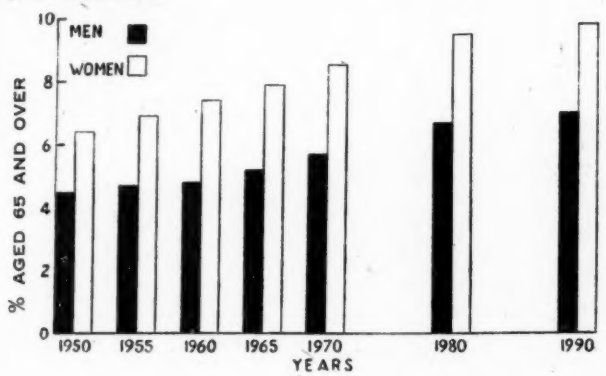
Disease	1951 Week Ending April 7					1950 Corresponding Week					1942–50 England & Wales Corresponding Week		
	(*a*)	(*b*)	(*c*)	(*d*)	(*e*)	(*a*)	(*b*)	(*c*)	(*d*)	(*e*)	Highest	Median	Lowest
Diphtheria	48	8	23	1	3	65	7	11	1	2	729	453	65
Deaths	1	—	—	—	—	—	—	—	—	—			
Dysentery	846	187	194	15	4	363	11	78	2	—	363	168	44
Deaths		—		—					—				
Encephalitis, acute	8	1	—	—		3	—	—	—	—	5	1	—
Deaths		—			—		—						
Erysipelas			19	3	3			24	6	6			
Food-poisoning	69	17		5		62	2		—				
Infective enteritis or diarrhoea under 2 years				10	21					10			
Deaths	13		3	1	—	21		1	—	—			
Measles*	28,800	2,083	593	188	164	5,487	91	196	424	90	22,599	8,343	2,268
Deaths		2	1	—	1			—	—	—			
Meningococcal infection	39	5	26	—	5	26	2	9	4	2	199	78	26
Deaths		—	—				3	—					
Ophthalmia neonatorum	34	3	11	—		28	3	10	1		92	67	28
Pneumonia, influenzal	799	36	10	15	9	698	24	9	13	—	1,297	967	693
Deaths (from influenza)†	49	7	1	—	3	117	22	1	1	6			
Pneumonia, primary			208					162					
Deaths	253	46		16	13	231	37		6	10			
Poliomyelitis, acute:													
Paralytic	11	—	} 2	}—	} 2	} 19	} 2	} 2	} 1	} 3	} 19	} 5	} 1
Non-paralytic	4	—											
Deaths§	1	—			—	3	—			—			
Puerperal fever			4				—	3					
Puerperal pyrexia‖	68	8	8	3		81	6	4	—		187	140	81
Scarlet fever	843	48	139	21	36	1,316	103	152	104	45	2,089	1,316	939
Deaths		—	—	—	—			—	—	—			
Smallpox	—	—	—	—		—	—	—	—				
Deaths				—					—				
(1) Tuberculosis, respiratory			154	25				130	30				
(2) Tuberculosis, non-respiratory			35	3				24	3				
(1) Deaths	} 175	{ 25	29	5	11	} 182	{ 24	28	1	14			
(2) Deaths		6	3	—	2		1	4	4	4			
Typhoid fever	8	1	3	—	2	1	—	2	—	1			
Deaths¶	—	—	—	—		—	—	—	—		14	9	4
Paratyphoid fever	27	—		—		3	—	1 (A) 2 (B)	—				
Whooping-cough	4,009	247	588	33	68	2,127	102	276	60	69	3,303	1,969	1,043
Deaths	6	—	2	—	1	3	—	—	1	—			
Deaths (0–1 year)	304	45	42	14	18	281	45	33	13	7	521	387	281
Deaths (excluding stillbirths)	5,817	906	673	161	223	5,322	797	536	137	172	5,784	4,972	4,522
Annual death rate (per 1,000 persons living)			13·6					10·8					
Live births	8,049	1,296	1,030	248	416	6,845	1,110	823	239	317	8,752	6,922	5,731
Annual rate per 1,000 persons living			20·8					16·5					
Stillbirths	189	26	39			161	20	35			285	226	161
Rate per 1,000 total births (including stillborn)			36					41					

* Measles not notifiable in Scotland and returns are approximate. † Includes primary form for England and Wales, London, and N. Ireland. § The number of deaths from poliomyelitis and polio-encephalitis for England and Wales, and London (administrative county), are combined. ‖ Includes puerperal fever for England and Wales and for Eire. ¶ Deaths from paratyphoid fever are combined with those from typhoid fever.

Vital Statistics

The Ageing Population

The Registrar-General has estimated the age structure of the population of England and Wales for the next 40 years in his fourth *Quarterly Return* for 1950. He starts from the estimated population at December 31, 1950, and then gives projections of the population in various age groups up to 40 years on, making certain assumptions about future mortality and natality and assuming that there is no migration. He finds that the number of children under 15 declines from 219 per 1,000 total population in 1950 to 202 per 1,000 in 1990. In the same period the number of men aged 65 and over increases from 45 to 70 per 1,000, and the number of women aged 60 and over from 91 to 126 per 1,000. The diagram below, which is based on his figures, shows the percentage of men aged 65 and over and of women aged 65 and over in the population of England and Wales in the years indicated.



Week Ending April 14

The notifications of infectious diseases in England and Wales during the week included: scarlet fever 822, whooping-cough 3,836, diphtheria 42, measles 22,644, acute pneumonia 707, acute poliomyelitis 20, dysentery 858, paratyphoid fever 13, typhoid fever 6. Deaths from influenza in the great towns numbered 33.

Review of 1949

The Registrar-General for England and Wales has made several small changes in his *Statistical Review* for the year 1949, just published. Areal comparability factors for the birth rate have been introduced to enable the birth rate in any specified area to be more accurately compared with that in any other area or in England and Wales as a whole. The numbers of stillbirths are now given for the administrative areas of the country, and also the numbers of neonatal deaths. Tables giving figures for both geographical regions and standard regions appear as before, but the Registrar-General announces that from 1950 standard regions will displace geographical regions in the main tables. There is a list of corrections to previous volumes that librarians should not overlook.

The following Table shows some figures taken from this *Review*. (Non-civilian males are excluded on and after September 3, 1939, non-civilian females on and after June 1, 1941.) Crude death rates at all ages per million living for the years 1939–49 are given for certain causes of death:

Causes of Death	1939	1940	1941	1942	1943	1944	1945	1946	1947	1948	1949
Diphtheria	52	62	68	47	36	24	18	11	6	4	2
Tuberculosis (all forms)	621	699	730	657	668	628	615	551	552	507	458
Cancer and other tumours	1,685	1,780	1,837	1,891	1,957	1,953	1,990	1,911	1,907	1,907	1,919
Rheumatic fever	23	21	16	13	17	16	14	9	9	10	8
Heart disease	3,052	3,416	3,145	3,049	3,185	3,278	3,354	3,286	3,460	3,152	3,579
Appendicitis	66	60	48	50	50	50	45	38	36	29	29

Infant Mortality in Various Countries

In 1950 the infant mortality rate in England and Wales was 30 per 1,000 live births, in the U.S.A. it was 29, and in the Netherlands 25 (Registrar-General's fourth *Quarterly Return*, 1950, England and Wales). The Registrar-General also gives figures comparing the experience of England and Wales with that of a number of other countries in 1948 and 1949. These figures are shown in the following table:

Deaths Under 1 Year Per 1,000 Live Births

Country	1948	1949
England and Wales	34	32
Scotland	45	41
Northern Ireland	46	45
Australia	28	25
Belgium	50	52
Canada	44	43
Chile	160	169
Denmark	35	34
France*	51	61
Irish Republic	49	59
Italy	70	74
Netherlands	29	27
New Zealand	22	24
Sweden	23	23
U.S.A.	32	31

* Rate for 1948 excludes liveborn infants who died before registration.

Births and Fertility in England and Wales

The course of the birth rate during the six war years 1940 to 1945 is reviewed in the Text, Volume 2, Civil, of the Registrar-General's *Statistical Review of England and Wales, 1940–5*. The birth rate in England and Wales, since the commencement of civil registration, was at a maximum during 1865–80, when the rate was slightly above 35 per 1,000 of the population. From this date, with the exception of the years immediately following the first world war, the rate declined continuously to a minimum of 14.4 per 1,000 in 1933. After 1933 the birth rate tended to rise very slightly, and a rate of 15.1 per 1,000 was recorded in 1938. A slight fall to 14.8 was recorded in 1939, but with the outbreak of war the rate declined still further to 14.1 per 1,000 in 1940 and to 13.9 in 1941; this was the lowest rate ever recorded in this country. From 1941 an unexpected and substantial increase began; in 1942 the birth rate rose to 15.6, in 1943 to 16.2, and in 1944 to 17.7. A temporary fall occurred in 1945, when the rate was 15.9 per 1,000. This fall may be associated with the withdrawal of large numbers of the Forces to the Continent for the invasion and also, to some extent, with the flying-bomb and rocket attacks on the south-eastern section of the country. With the end of the war, the birth rate increased rapidly and a rate of 19.2 was recorded in 1946 and 20.5 in 1947, the highest level that the birth rate has attained since 1921.

The course of the birth rate during 1940–5 was in contrast to that experienced during the first war of 1914–18. In the first war the birth rate fell continuously during the years of hostilities from 24.1 in 1913 to 17.7 in 1918. This fall was followed by a temporary boom when war ended, and rates of 25.5, 22.4, and 20.4 were recorded in 1920, 1921, and 1922.

The difference between the trends in the two wars is interesting. Judging from the experience of 1914–18 a fall in the birth rate such as occurred in the first two years of the last war and a boom following the termination of hostilities were to be expected. But a satisfactory reason why the birth rate should have commenced to rise

continuously as early as 1941 has not been advanced. There was a different disposition of the armed Forces: in the first war the bulk of the men of military age served abroad for long periods, while for the first years of the last war a large proportion were stationed in the country; this may have been a factor of importance. A boom in marriages may also have been partly responsible; the marriage rate jumped from 17.6 per 1,000 of the population in 1938 to 21.2 in 1939. This rate was markedly higher than any similar rate since official registration was introduced more than 100 years ago. The high marriage rate of 1939 was exceeded in 1940, when the rate reached 22.5 per 1,000. This large increase in the number of marriages meant that the average age of the women marrying decreased and consequently they were of a more fertile age. Differences in the circumstances of the two wars can hardly account for the varying trends of the birth rate over the two periods. The upward trend in the birth rate was not confined to this country but occurred in other countries, neutral and belligerent, where the birth rate had declined during the two wars.

The illegitimate birth rate varied considerably in the two war periods. During the four years 1911–14 the illegitimate birth rate was 8.0 per 1,000 single and widowed women aged 15 to 44, and it remained fairly constant during the war with rates of 7.6, 7.8, 7.7, and 8.5 for the four years 1915 to 1918. In the six years 1934–9 preceding the second war the illegitimate birth rate had fallen to 5.5, but a steady and marked increase was recorded in each of the war years. The rates were 5.9, 7.4, 9.0, 10.9, 13.8, and 16.1 for 1940 to 1945.

The effective reproduction rate, a rate designed to take into account the sex–age characteristics of the population, shows the proportion which the births actually recorded in a year had to the number theoretically required to maintain the existing population. This rate was 0.808 in 1939—that is, 19% below the full replacement standard. The rate fell to a minimum of 0.761 in 1941 and then rose above the replacement level in 1946 to 1948 with values of 1.103, 1.205, and 1.070. For the nine years 1940–8 the average effective reproduction rate was 0.952, less than 5% short of full replacement standard but considerably above the pre-war level. Several factors affect the effective reproduction rate, but the main factor determining the fertility of a population is the rate at which the average married woman bears children. The marriage influence, through the boom in marriages and marriages at a lower average age, has provided a large positive but temporary contribution to the rate. Fertility is at a maximum during the first year of married life and then steadily declines with each further year of duration. Improvement in survivorship mortality still exercises a small positive influence, but the contribution in recent years has been insignificant; in 1911–22 survivorship mortality contributed an increase of 0.076, but in 1946–7 the increase was only 0.002.

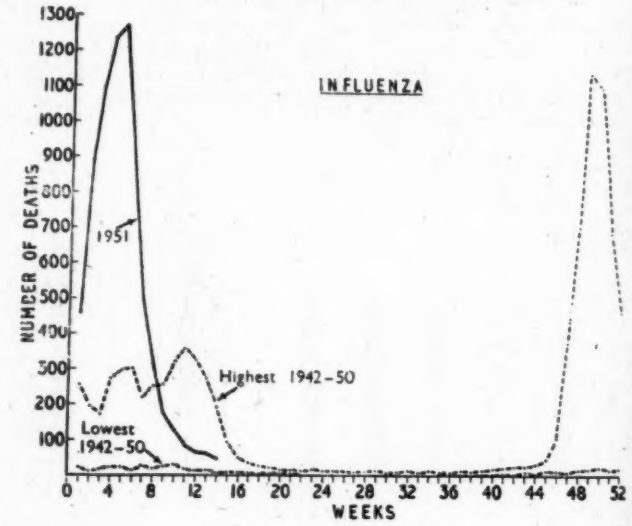
The stillbirth rate in 1928 (the first complete year of registration) was 40.1 per 1,000 total births. Until the war the rate remained high, with only a slight tendency to decline; the rate in 1938 and 1939 was over 38. The rate fell steadily during the war, and in 1945 it was 27.6. The neonatal death rate only showed a small fall from 20.5 in 1939 to 17.6 in 1945. The chance of children being born alive had improved considerably, but the chance of surviving the first month of life had not improved to the same extent.

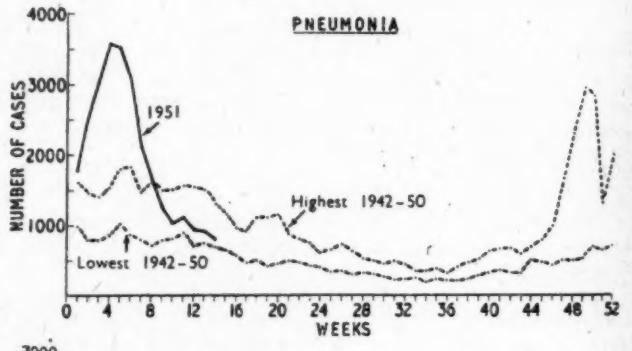
There were 59,300 twin births, 496 triplet, and 9 quadruplet maternities during 1938–45; 8,000 of the 120,124 births from multiple maternities were stillborn. The probability of a multiple birth increased with age of mother from 6.38 per 1,000 maternities at ages under 20 to a maximum of 16.83 at ages 35 to 39 and then declined. One maternity in 84.0 produced twins, and 1 in 10,037 resulted in triplets. There was a regional variation in the proportions of multiple maternities, and the chance of a multiple birth was greatest in the north and least in the south-east.

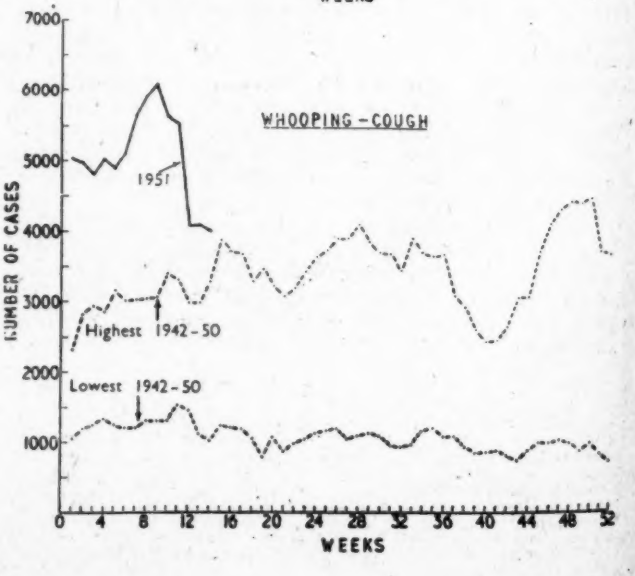
The sex ratio at birth, during 1938–45, was 1,059 males to 1,000 females. There was a regular progression with age of mother. The ratio was 1,068 for mothers under 20, and it continuously declined with advancing age to 1.030 at ages 45 and over.

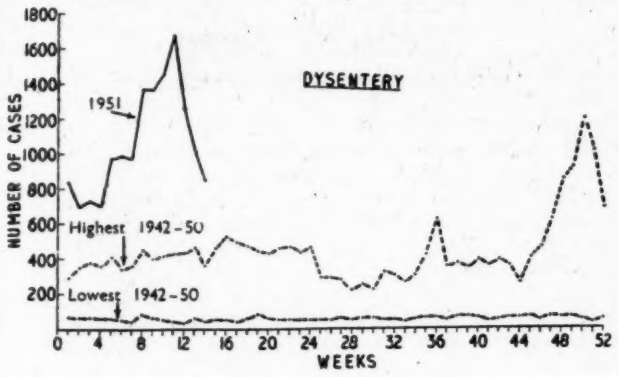
Graphs of Infectious Diseases

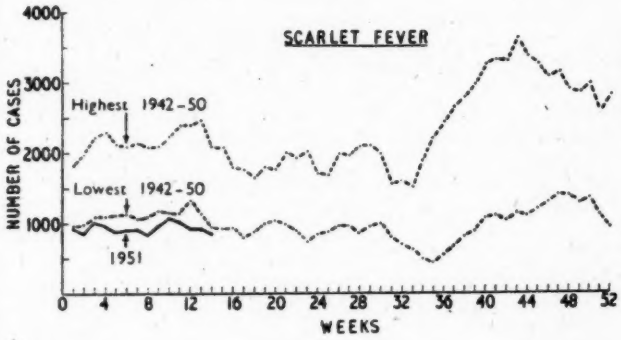
The graphs below show the uncorrected numbers of cases (deaths from influenza) of certain diseases notified weekly in England and Wales. Highest and lowest figures reported during the nine years 1942–50 are shown thus - - - - - -, the figures for 1951 thus ————. Except for the curves showing notifications in 1951, the graphs were prepared at the Department of Medical Statistics and Epidemiology, London School of Hygiene and Tropical Medicine.

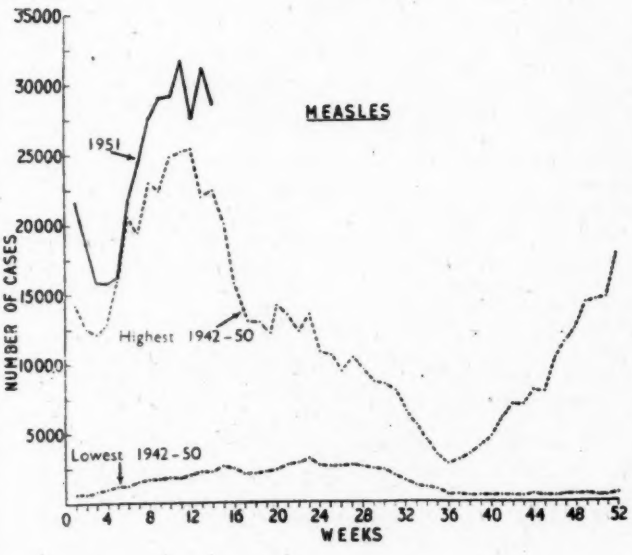












Infectious Diseases

During the week ending April 7 a fall in the number of notifications was recorded in England and Wales for measles 2,468, acute pneumonia 110, dysentery 153, whooping-cough 89, and scarlet fever 75.

The notifications of measles fell by over 100 in 13 counties, the greatest decline in incidence being centred on London and the adjacent counties. The largest falls in the number of notifications of measles were Middlesex 429, Essex 339, London 277, while the largest exceptions to the general decline in incidence were rises in Warwickshire 317, Yorkshire West Riding 190, and Leicestershire 145. The largest decreases in the number of notifications of whooping-cough were Essex 74, Devon 65, Kent 64, and the largest increases were Yorkshire West Riding 52 and London 49. There was little variation in the local returns of scarlet fever. The chief fluctuations in the trends of diphtheria were a rise of 5 in London and a fall of 5 in Staffordshire. In Scotland 23 cases of diphtheria were notified, the largest return for 12 months; 12 of these cases were notified in Glasgow.

Of the 35 cases of typhoid and paratyphoid fever 11 were notified in Lancashire, 6 in Staffordshire, and 6 in Durham. The only multiple cases of poliomyelitis were Lancashire 3 (Liverpool C.B. 2) and Yorkshire West Riding 2. A fall in the incidence of dysentery was recorded for the fourth consecutive week, but the incidence is still very high. The largest returns were London 187 (Islington 48), Lancashire 116, Middlesex 84, Essex 53, Yorkshire West Riding 51, Lincolnshire 43 (Scunthorpe M.B. 34).

Eight deaths were classified as due to smallpox in January. Two of these deaths occurred in Brighton C.B., three in Portslade-by-Sea U.D., and three in Dartford U.D.

Universities and Colleges

UNIVERSITY OF OXFORD

Mr. V. E. Negus will deliver a Litchfield Lecture on "Defences of the Air Passages, with Relation to Ciliary Action" at the Radcliffe Infirmary, Oxford, on Wednesday, May 16, at 5 p.m.

Professor E. Harlan Wilson, Columbus University, U.S.A., will deliver a lecture on "Fundamentals Related to Surgical Procedures in Orthopaedic Surgery" in the Nuffield Department of Orthopaedic Surgery, Oxford, on Thursday, May 10, at 8.30 p.m.

UNIVERSITY OF CAMBRIDGE

The Linacre Lecture on "The University and Clinical Medicine" will be delivered by Sir James Spence, M.D., F.R.C.P., Professor of Child Health in the University of Durham, in the lecture room of the Anatomy School on Saturday, May 5, at 5 p.m.

UNIVERSITY OF ST. ANDREWS

Donald Macleod Douglas, Ch.M., F.R.C.S., Reader in Experimental Surgery in the University of Edinburgh and Deputy Director of the Wilkie Surgical Research Laboratory, has been appointed to the Chair of Surgery in the University of St. Andrews.

John Louis Henderson, M.D., F.R.C.P.Ed., Senior Lecturer in the Department of Child Life and Health in the University of Edinburgh and physician at the Royal Hospital for Sick Children, Edinburgh, has been appointed to the James Mackenzie Chair of Child Health in the University of St. Andrews.

UNIVERSITY OF BRISTOL

The following candidates have been approved at the examination indicated:

DIPLOMA IN MEDICAL RADIODIAGNOSIS.—*Part II:* Sheila M. Cameron, A. G. M. Davies.

ROYAL COLLEGE OF SURGEONS OF ENGLAND

At a meeting of the Council of the College, held on April 12, with Sir Cecil Wakeley, President, in the chair, a Past-President's Badge was presented to Sir Hugh Lett.

Mr. C. D. Read was admitted to the Fellowship of the College *ad eundem*.

The Leverhulme Research Scholarships of Mr. A. T. Andreasen and Mr. L. I. Williams were renewed for a further year. The Begley Prize for 1951 was awarded to G. L. Howe (Middlesex Hospital). The Council selected "The Surgical Treatment of Carcinoma of the Stomach" as the subject for the Jacksonian Prize for 1952.

The Walker Prize of £100 for 1946–50 was awarded to Professor Alexander Haddow, Professor of Experimental Pathology in the University of London and Director of the Chester Beatty Research Institute, for his many notable contributions in the field of chemotherapy of cancer, for his leadership and organization in directing a great institute for cancer research, and for the high regard in which he is held by cancer research workers in this country and abroad.

The following were elected to the Fellowship of the College without examination as being medical practitioners of at least 20 years' standing: A. H. Harkness, M. C. Wilkinson, I. W. Magill, A. O. Parker, Surgeon Captain R. W. Higgins, R.N., and Professor Thomas Nicol.

Dr. James Craigie, F.R.S., and Professor Alexander Haddow were appointed Imperial Cancer Research Fund Lecturers for 1951.

Diplomas in Physical Medicine, in Ophthalmology, in Tropical Medicine and Hygiene, and in Child Health were granted, jointly with the Royal College of Physicians of London, to the following successful candidates:

DIPLOMA IN PHYSICAL MEDICINE.—M. Q. Birkbeck, B. O. Scott.

DIPLOMA IN OPHTHALMOLOGY.—G. W. Allen, C. H. Baker, H. H. W. Bennett, G. L. Cantrell, M. Cowan, J. A. Eustace, E. M. L. Evans, R. H. L. Ferguson, A. R. Gabbay, F. A. Hamdi, D. R. Ll. Hart, J. J. Heany, H. K. Indra, N. C. Jain, J. McLenachan, J. G. Madden, K. P. Milne, T. G. O'Driscoll, Winifred I. Pearce, R. P. Phillips, N. Pines, M. A. Qayyum, M. Q. K. Raja, J. Roche, J. H. Slade, Mona A. Smith, L. C. G.-L. Trichard, J. Whitwell, Kin Yip Wong.

DIPLOMA IN TROPICAL MEDICINE AND HYGIENE.—W. G. L. Allan, I. N. O. Asinobi, J. C. Babbage, Bo Kyaw, M. A. Botawala, J. Carswell, D. W. F. Charlton, B. J. Chelmicki, V. St. E. D'Abrera, C. R. Doering, A. C. Doshi, F. Elahi, T. Fernando, L. F. Gunaratna, B. P. Harris, H. Herlinger, J. H. Hobson, Ma Hpay, V. Israngura, L. Kant, I. S. Khutaina, K. D. Lahiri, Poo Ling, J. A. McDonald, W. H. McDonald, J. A. Mahoney, A. L. Meikle, H. O. L. Murray, R. J. Pitchford, B. Prasad, S. Singh, L. P. Spence, D. A. Thamotheram, M. Yildiz.

DIPLOMA IN CHILD HEALTH.—H. Altman, J. P. Anderson, G. C. Arneil, S. L. Balse, J. S. Beedie, Mary T. Behanan, S. K. Biswas, S. K. Bose, Lucy McL. C. Boyd, R. J. K. Brown, H. Chai, Isabel A. Cossar, Constance M. Cowan, Mary E. Curling, S. B. du Toit, J. S. Ebsworth, R. E. E. Edwards, J. Erulkar, D. G. Evans, Elspeth M. Evans, Loveday A. Farquharson, Ann Ferguson, Prudence A. FitzGerald, R. M. Forrester, J. B. Frost, Angela D. Fuller, Molly I. Govier, A. J. Gray, Zaida M. Hall, Yuen Ho, C. W. Howden, L. S. Jaikaran, T. K. Jari, J. G. P. Jones, S. M. A. Khadri, P. Lancer, K. W. Lavers, Lois M. Leitch, S. Levin, Joan V. Llewelyn, A. Macfarlane, Lisa E. Mandelbaum, Margaret G. Martin, Joan M. Milne, Mary D. Milne, L. H. Mofflin, Judith Murray-Jones, R. W. Nash, Margaret I. E. Neave, G. F. Newbold, Joan R. Nichols, Marjorie G. Nisbet, T. C. Noble, F. H. Patel, K. Rajasuriya, Margaret P. B. Reid, J. D. L. Reinhold, Jean Robson, F. C. Rose, Margaret M. P. Ryan, H. Sharma, S. Skulthai, Mary G. Southern Holt, Sybil H. Stephens, G. J. Sutin, H. T. Swan, Joyce M. Teasdale, Joan P. Tom, S. B. Vahidy, S. Vaishnava, R. H. Vines, Mary Vowles, Daphne M. L. Walters, B. W. Webb, J. W. Woodburn, Audrey J. Worman, Guan Eng Yeoh.

DIPLOMA IN PSYCHOLOGICAL MEDICINE.—J. B. Gordon Russell.

DIPLOMA IN INDUSTRIAL HEALTH.—D. Crichton.

The following hospitals were recognized under paragraph 23 of the F.R.C.S. regulations: Caernarvonshire and Anglesey General Hospital, Bangor (surgical registrar, first and second house-surgeons, all for six months); Leicester Royal Infirmary (five house-surgeons—general, orthopaedic house-surgeon, and house-surgeon to ear, nose, and throat departments—all for six months); St. Leonard's Hospital, London (two house-surgeons for six months).

The Services

Major-General R. D. Cameron, C.B.E., M.C., late R.A.M.C., has been appointed Honorary Surgeon to the King in succession to Major-General W. E. Tyndall, C.B., C.B.E., M.C., K.H.S., retired.

Brigadier W. R. D. Hamilton, O.B.E., late R.A.M.C., has been appointed Honorary Physician to the King in succession to Major-General J. Bennet, retired.

The name of Captain C. W. Bowen, R.A.M.C., appears in a *London Gazette* in a list of those awarded the Military Cross in recognition of gallant and distinguished services in Korea during the period July 9 to December 31, 1950.

A *Supplement* to the *London Gazette* has announced the following awards:

Four Clasps to the Territorial Efficiency Decoration.—Honorary Brigadier H. L. Garson, O.B.E., M.C., T.D., R.A.M.C., retired, and Colonel J. W. Hirst, O.B.E., T.D., R.A.M.C.

Three Clasps to the Territorial Efficiency Decoration.—Major (Honorary Lieutenant-Colonel) J. C. Barrett, V.C., T.D., R.A.M.C.

First Clasp to the Territorial Efficiency Decoration.—Lieutenant-Colonel (Brevet-Colonel) G. A. Kane, O.B.E., T.D., R.A.M.C., and Captain (Honorary Major) J. N. Martin, T.D., R.A.M.C., retired.

Territorial Efficiency Decoration and First Clasp.—Majors E. F. Baines and W. Kelly, R.A.M.C.

Territorial Efficiency Decoration.—Majors A. McArthur and W. F. Mair, and Captain (Honorary Lieutenant-Colonel) N. H. Martin, R.A.M.C.; Honorary Major P. S. L. Finlayson, R.A.M.C., retired.

Medical News

Medical Service in Korea

The United States Army in Korea is providing medical services not only for its own troops but for the two British and one Turkish brigades in action there, as well as for the forces (roughly a battalion each) contributed by France, the Netherlands, Greece, Thailand, Belgium, the Philippines, Australia, Canada, and New Zealand. Apart from an Indian medical unit and the Swedish Red Cross hospital there are three evacuation hospitals, five mobile surgical hospitals, four field hospitals, two 500-bed station hospitals, and several hospital ships. Since Japan is only 140 miles away (45 minutes' flying time) patients can be moved out of Korea at once if they are likely to be long-term cases. Forward evacuation is by jeep ambulance, field ambulance, and helicopter to the mobile surgical hospital, and thence by train, since 62 ambulance railway coaches have been shipped in. Most of the evacuation from Japan to the U.S.A. is by air, often now in two 16-hour hops, landing at Hawaii and then near San Antonio, Texas. For British and French casualties the R.A.F. provide transport home via Singapore and the Middle East. The mortality rate of the wounded in hospital is said to be 2½%, compared with 4% in the second world war and 8% in the first world war. The cold winter of Korea has provided some problems, and specially selected N.C.O.s have been made responsible for cold-weather discipline; among other duties they give permission for individual men to return to a warming-tent. For the wounded, plastic bags which can be slipped over blankets to cut down wind chill are being developed. The great bulk and weight (34 lb.—15.3 kg.) of the early model makes it unsuitable for forward use, but a new version weighing only 13 lb. (5.9 kg.) is due for test.

Research at the Buckston Browne Farm

At a reception held at the Buckston Browne Research Farm of the Royal College of Surgeons on March 30, Professor A. Sorsby spoke on retinal dystrophy in Irish setters, Mr. A. T. Andreasen on blood flow in the azygos vein after caval obstruction in dogs, Dr. D. Melrose on an artificial heart-lung, Mr. W. J. Dempster on transplantation of the kidney, Dr. I. G. Graber on the effect of unilateral adrenalectomy on the function of the kidney of the same side, and Dr. K. Digby on the function of the lymphoid tissue in the rabbit's appendix.

Prize Essay Competitions

The council of the Royal Sanitary Institute has announced particulars of the prize essay competitions for 1951. Two prizes are offered: the John Edward Worth Prize of £40 for an essay on "The Planning of Old People's Dwellings and the Provision of Communal Facilities and Services in Connexion Therewith," and the John S. Owens Prize of £15 for an essay on the ventilation of dwellings and its effect upon human health. Intending competitors should apply to the Royal Sanitary Institute, 90, Buckingham Palace Road, London, S.W.1, for a copy of the general conditions. Entries must be submitted by December 31.

Foreign Members of the Royal Society

At a meeting of the Royal Society on April 19 the following were elected: Herbert McL. Evans (Berkeley, Cal.), aged 69, noted for his work on endocrinology, the discoverer of vitamin E, of pituitary growth hormone, and A.C.T.H.; Karl S. Lashley (Cambridge, Mass.), aged 61, distinguished for his studies of the neurological basis of animal behaviour and of learning; Carl Störmer (Oslo), an authority on the motion of charged particles in magnetic fields and on the aurora borealis; and R. W. G. Wyckoff (Bethesda, Md.), aged 53, a crystal physicist and electron microscopist, who has recently contributed greatly to knowledge of viruses and bacteriophage.

"Family Doctor"

The May issue of *Family Doctor* was published yesterday. Special features in this number are an article by a general practitioner entitled "Ought I to See a Specialist?" and one by Professor Alan Moncrieff on "Children in Hospital." There is a full description of London's new Royal Festival Hall and a general article on "Music and Medicine." Other contributions are on colour-blindness, children's teeth, glass eyes, and swallowed foreign bodies. There is a gardening article, a note about measles, and the usual sections on cookery, prospective motherhood, and baby care. Phrenology is discussed under the heading "Old Wives' Tales," and there are short articles on backache, streptomycin and P.A.S., smallpox, and the health problems of Korea. Copies can be ordered from any newsagent or direct from the Publishing Manager at B.M.A. House.

Society for Endocrinology

At the annual general meeting of the Society on April 12 Dr. S. J. Folley was elected chairman, Professor C. H. Gray and Dr. N. M. Maclagan honorary secretaries, and Dr. F. L. Warren honorary treasurer. Professor S. Zuckerman was elected editor of the *Journal of Endocrinology*. He is to be assisted by Dr. P. L. Krohn.

W.H.O. News

Spain, the German Federal Republic, and Japan will be considered for membership of the World Health Organization at its fourth world assembly, Geneva, May 7. New international sanitary regulations will also be considered, reducing quarantine restrictions and providing for periodical revision of the regulations. For the first time relapsing fever appears in them as a disease for international control.

Annotated Bibliography of Cortisone

The second issue of this quarterly abstracting bulletin is now available from the Empire Rheumatism Council, Tavistock House (North), Tavistock Square, W.C.1, at a price of 5s. In its 35 pages it covers the literature in English on cortisone and A.C.T.H. from the previous bulletin up to November, 1950.

Rare Gas as Anaesthetic

Xenon, one of the rare gases present in the atmosphere, is used commercially to fill the tubes of some so-called neon signs—it gives a green light—and occurs as a by-product in the manufacture of liquid air and oxygen. According to the British United Press it has now been used with success as an anaesthetic in four major surgical operations at the State University of Iowa. It is non-inflammable and chemically inert, and both induction and recovery are rapid. Presumably its only physiological effect is a controllable anoxia.

Potassium Bromide

The Ministry of Health states that, as a temporary measure, sodium bromide may be dispensed instead of the potassium salt where supplies of the latter are not available to meet orders on N.H.S. prescriptions. No special endorsement of prescriptions is required.

Police Surgeons Association of Great Britain

The Metropolitan Police Surgeons Association has decided to extend membership to doctors engaged in police work outside the Metropolitan area and, therefore, to change the name of the association. The inaugural general meeting of the new association will be held at New Scotland Yard, London, S.W.1 (Room 386, North Extension), on Wednesday, May 2, 1951, at 3 p.m., and is open to all interested and eligible—about 190 police surgeons have already applied for membership.

Saying of the Week

Mr. Aneurin Bevan, speaking in the House of Commons on charges for spectacles and dentures: "Has the A.M.A. succeeded in doing what the B.M.A. failed to do?"

Wills

Dr. Geoffrey Stanger, in practice at Heathfield, left £9,704. Mr. Cyril Edward Alfred Bedwell, honorary member of the Middle Temple and keeper of the library, 1909–21, late chairman of Camberwell Hospitals Management Committee, and a former house governor and secretary of King's College Hospital, left £9,423. Lieutenant-Colonel Sir Thomas Reginald St. Johnston, of Belsaye, Ratton Road, Eastbourne, a former Governor of the Leeward Islands, soldier, barrister, doctor, and author, left £7,274. Professor Walter James Dilling, professor of pharmacology at the University of Liverpool, chairman of the Liverpool Philharmonic Society, 1937–40 and 1945–8, left £5,208. Mr. Norman Stuart Carruthers, formerly in charge of the ear, nose, and throat department of the Norfolk and Norwich Hospital, left £28,147. Dr. Horace Richardson, of Worthing, left £8,991. Dr. Eric Barlow Brown, a former senior surgeon at Oldham Royal Infirmary, left £44,752.

Colonel Thomas Fraser, consulting physician to the Aberdeen Royal Infirmary and President of the British Medical Association from 1939 to 1942, left estate valued at £22,373. Dr. John Rippiner Heath, of Barmouth, well known as a composer of orchestral music, conducting his own compositions at the 1922 promenade concerts in London, left £9,203.

Dr. William Lowson left £42,391. Dr. Douglas Edward Finlay, a former Mayor of Gloucester and for 10 years chairman of the Gloucester Education Committee, left £648. Dr. Edward Gillespie, for many years a member of the surgical staff of the Prince of Wales General Hospital, Tottenham, and surgeon to Tottenham Hotspur F.C., left £17,007. Surgeon Captain Percy Montgomery Rivaz, late senior medical officer at Chatham Dockyard, and afterwards in practice at Lewisham and doctor at the R.F.A. Orphanage, Vanbrugh Castle, left £11,071. Dr. Richard Charles Lowther, a practitioner of Grange-over-Sands, Lancs, a keen naturalist and a member of the Royal Society for the Protection of Birds and other societies, left £34,574. Dr. Harold Ernest Rawlence, formerly of Southampton, left £19,700.

Mr. Frederick Lindsay-Dickson, formerly in practice at Shanklin, and at Wing, Bucks, left £12,665. Dr. Alfred Kaye Jarratt, of Bridlington, left £12,461.

Dr. Florence Slade (or Louis), a consultant pathologist, of London, N.W.3, left £17,202. Dr. Robert Turnbull Easton Naismith, of Slaithwaite, near Huddersfield, left £11,022.

Dr. John Broadley, for 26 years honorary surgeon at Sheffield Children's Hospital, left £31,313. Dr. Henry Dean Haworth, honorary physician to the Victoria Hospital, Burnley, and for many years in general practice in Nelson, left £34,494.

He left his residence and effects to his wife and the residue upon trust for her for life and then £100 to his godson, and one-third of the remainder to his sister or her children, and two-thirds of the remainder to the Victoria University of Manchester, to establish a scholarship or scholarships for the benefit of such deserving scholars of either sex at the Nelson Secondary School as are desirous of continuing their education at the said University.

COMING EVENTS

International Haemophilia Society

The Society will hold a meeting on Sunday, April 29, at 2.30 p.m., at the Society for Visiting Scientists, 5, Old Burlington Street, W.1. Members of the medical profession as well as haemophilic families will be welcome at the meeting, which is intended to be a social gathering.

Contraceptive Technique

A lecture and demonstration (on living models) on contraceptive technique will be given by Dr. Marie Stopes, Ph.D., at the Mothers' Clinic, 108, Whitfield Street, London, W., on Thursday, May 3, at 2.30 p.m. Tickets must be obtained in advance as space is limited.

Hackney Hospital

The Duchess of Gloucester will open the maternity wing of Hackney Hospital on Wednesday, May 2, at 3 p.m.

Conference on Occupational Therapy

The Association of Occupational Therapists will hold a two-day conference on the aims and scope of occupational therapy at the Hoare Memorial Hall, Church House, Westminster, on June 15 and 16, at which it is hoped many visitors from overseas will be present. Further particulars may be obtained from the secretary, 251, Brompton Road, London, S.W.3.

Conference on Disorders of Oesophagus and Duodenum

Meetings on Saturday and Sunday, June 16 and 17, are being held in the Faculty of Medicine, Paris, organized by the Société Nationale Française de Gastro-entérologie, and full information can be obtained from Dr. F. Moutier, 78, rue de Monceau, Paris, 8e.

Seventh International Hospital Congress

As previously announced, the International Hospital Federation is holding the Seventh International Hospital Congress in Brussels, July 15–21, on the theme of "Care of the Chronic Sick and Aged." The fee for members of the I.H.F. is 210 Belgian francs, for members' relations 140 Belgian francs, and for non-members 350 Belgian francs. Further details may be obtained from Athénée Robert Catteau, rue Ernest Allard, Brussels.

Congress of Anaesthetists

The 26th Annual Congress of Anaesthetists will be held in London from September 3 to 7, at British Medical Association House, Tavistock Square, London, W.C.1. There will be a registration fee of £2 2s. Copies of the programme may be obtained from the Congress Secretary, 25, Park Crescent, London, W.1, to whom all inquiries should be addressed.

Tenth International Congress of Industrial Medicine

The Congress will be held in Lisbon, September 9 to 15. The complete programme will be published in due course and sent to each delegate before the opening of the Congress. All inquiries should be addressed to the secretary of the Congress, Instituto Nacional do Trabalho e Previdência, Praça do Comércio, Lisbon.

Second European Congress of Rheumatology

Organized on behalf of the Ligue Européenne contre le Rhumatisme by the Spanish Society of Rheumatology, a four-day meeting is being held in Barcelona, September 24–27, with contributions from British, French, Swiss, German, Dutch, United States, and other workers. Full information may be obtained from the general secretary, Vía Layetana, 31, Casa del Medico, Barcelona, Spain.

SOCIETIES AND LECTURES

A fee is charged or a ticket is required for attending lectures marked ●. Application should be made first to the institution concerned.

Monday

INSTITUTE OF OPHTHALMOLOGY, Judd Street, London, W.C.—April 30, 5.30 p.m., *"Physico-chemical Aspects of Vision,"* by Dr. H. J. A. Dartnall.

INSTITUTE OF PSYCHIATRY, Maudsley Hospital, Denmark Hill, London, S.E.—April 30, 5.30 p.m., lecture-demonstration by Dr. E. Stengel.

ROYAL EYE HOSPITAL, St. George's Circus, Southwark, London, S.E.—April 30, 5 p.m., *"Antibiotics,"* by Professor Arnold Sorsby.

Tuesday

EDINBURGH POSTGRADUATE BOARD FOR MEDICINE.—At Anatomy Lecture Theatre, University New Buildings, May 1, 5 p.m., *"Intracranial Thrombophlebitis,"* by Sir Charles Symonds.

●INSTITUTE OF DERMATOLOGY, Lisle Street, Leicester Square, London, W.C.—May 1, 5 p.m., *"Psoriasiform Eruptions,"* by Dr. F. R. Bettley.

ROYAL EYE HOSPITAL, St. George's Circus, Southwark, London, S.E.—May 1, 5 p.m., *"The Phorias: Introduction to Orthoptics,"* by Dr. T. H. Whittington.

UNIVERSITY COLLEGE, Chemistry Lecture Theatre, Gower Street, London, W.C.—May 1, 5.30 p.m., *"Recent Advances in the Chemistry of Natural Products,"* first of three Special University Lectures by Professor R. B. Woodward, Ph.D. (Harvard University). (See also May 3 and 7.)

Wednesday

●INSTITUTE OF DERMATOLOGY, Lisle Street, Leicester Square, London, W.C.—May 2, 5 p.m., *"Acute Inflammation,"* by Dr. J. O. Oliver.

INSTITUTE OF OPHTHALMOLOGY, Judd Street, London, W.C.—May 2, 5.30 p.m., *"Electro-physiology of the Retina,"* by Dr. L. C. Thomson. (Demonstration in three groups.)

LONDON SCHOOL OF HYGIENE AND TROPICAL MEDICINE, Keppel Street, Gower Street, W.C.—May 2, 5.30 p.m., *"Obstetric Trends in a Changing Society,"* Newsholme Lecture by Professor Dugald Baird (see also May 3 and 4).

Thursday

EDINBURGH UNIVERSITY, University New Buildings (Anatomy Theatre), Teviot Place, Edinburgh.—May 3, 5 p.m., *"The Muscular Tone of the Gastro-intestinal Tract,"* Honyman Gillespie Lecture by Dr. John B. King.

●INSTITUTE OF DERMATOLOGY, Lisle Street, Leicester Square, London, W.C.—May 3, 5 p.m., *"Physio- and Electro-therapy,"* by Dr. R. T. Brain.

LONDON SCHOOL OF HYGIENE AND TROPICAL MEDICINE, Keppel Street, Gower Street, W.C.—May 3, 5.30 p.m., *"Obstetric Trends in a Changing Society,"* Newsholme Lecture by Professor Dugald Baird (see also May 2 and 4).

ROYAL ARMY MEDICAL COLLEGE, Millbank, London, S.W.—May 3, 5 p.m., *"Episodes from the History of Military Medicine,"* by Dr. W. R. Bett.

ROYAL COLLEGE OF SURGEONS OF ENGLAND, Lincoln's Inn Fields, London, W.C.—May 3, 5.30 p.m., *"Malignant Disease of the Tongue and Buccal Cavity,"* otolaryngology lecture by Sir Stanford Cade.

ROYAL EYE HOSPITAL, St. George's Circus, Southwark, London, S.E.—May 3, 5 p.m., *"The Interpretation of Skull and Orbital X-ray Films,"* by Dr. A. M. Rackow.

ST. ANDREWS UNIVERSITY.—At Lecture Theatre, Materia Medica Department, Medical School, Small's Wynd, Dundee, May 3, 5 p.m., *"The Pharmacology of Heart Failure in Man,"* by Professor J. McMichael.

ST. GEORGE'S HOSPITAL MEDICAL SCHOOL, Hyde Park Corner, London, S.W.—May 3, 4.30 p.m., *"Psychiatry,"* lecture-demonstration by Sir Paul Mallinson.

UNIVERSITY COLLEGE, Chemistry Lecture Theatre, Gower Street, London, W.C.—May 3, 5.30 p.m., *"Recent Advances in the Chemistry of Natural Products,"* second of three Special University Lectures by Professor R. B. Woodward, Ph.D. (Harvard University). (See also May 1 and 7.)

UNIVERSITY COLLEGE, Physiology Theatre, Gower Street, London, W.C.—May 3, 4.45 p.m., *"Energy Transformations in Living Matter,"* by Professor H. A. Krebs.

Friday

●INSTITUTE OF DERMATOLOGY, Lisle Street, Leicester Square, London, W.C.—May 4, 5 p.m., lecture-demonstration.

INSTITUTE OF OPHTHALMOLOGY, Judd Street, London, W.C.—May 4, 5.30 p.m., *"Further Observations on Contact Lenses,"* by Mr. F. Ridley.

LONDON SCHOOL OF HYGIENE AND TROPICAL MEDICINE, Keppel Street, Gower Street, W.C.—May 4, 5.30 p.m., *"Obstetric Trends in a Changing Society,"* Newsholme Lecture by Professor Dugald Baird (see also May 2 and 3).

●LONDON UNIVERSITY.—At Middlesex Hospital (Clinical Lecture Theatre), London, W., May 4, 4 p.m., *"The Chemical Manipulation of Food,"* Sanderson-Wells Lecture by Sir Edward Mellanby, F.R.S.

ROYAL COLLEGE OF SURGEONS OF ENGLAND, Lincoln's Inn Fields, London, W.C.—May 4, 5 p.m., *"Clinical and Experimental Investigation of the Circulation of the Liver (With Practical Application to General Surgery),"* Moynihan Lecture by Dr. Howard Gray (Mayo Clinic).

ROYAL EYE HOSPITAL, St. George's Circus, Southwark, London, S.E.—May 4, 4.30 p.m., *"Theatre Preparation and Post-operative Procedure,"* by Mr. A. J. Cameron.

Saturday

BIOCHEMICAL SOCIETY.—At Department of Biochemistry, University of Oxford, South Parks Road, Oxford, May 5, 11 a.m., 297th meeting. Papers will be read.

CAMBRIDGE UNIVERSITY, Anatomy School, Cambridge.—May 5, 5 p.m., *"The University and Clinical Medicine,"* Linacre Lecture by Sir James Spence.

APPOINTMENTS

Dr. Isaac Newton has been reappointed an Official Member of the Legislative Council of Hong Kong.

EASTERN REGIONAL HOSPITAL BOARD.—*Consultant Assistant Surgeons, Eastern Regional Orthopaedic Service*, James Hutchison, M.B., Ch.B., F.R.C.S.Ed., and I. D. Sutherland, M.D., F.R.C.S.Ed. *Part-time Ophthalmologist (Senior Hospital Medical Officer)*, H. E. Walker, M.B., Ch.B., D.O.M.S.

EDWARDS, C. G., M.B., Ch.B., D.M.R.(D.), Consultant Radiologist, North Staffordshire Royal Infirmary.

HILSON, DON, M.B., M.R.C.P., M.R.C.P.Ed., D.C.H., Consultant Paediatrician, Oldham and Ashton areas, Manchester Regional Hospital Board.

HOSPITAL FOR SICK CHILDREN, Great Ormond Street, London, W.C.—*Assistant Resident Medical Officer, Tadworth Court (Senior House Officer Grade)*, Prudence A. Fitzgerald, M.B., Ch.B., *House-physicians (Senior House Officer Grade)*, H. McC. Giles, M.B., B.Chir., M.R.C.P., D.C.H., A. W. N. Oatway, M.B., B.Chir., M.R.C.P., R. H. Vines, M.R.C.P., D.C.H. *House-surgeon to Orthopaedic and Plastic Departments (Senior House Officer Grade)*, W. D. Smith, M.B., B.Ch., B.A.O. *Surgical Registrar (Senior Registrar Grade)*, N. K. Connolly, M.D., F.R.C.S. *Part-time Orthopaedic Registrar (Registrar Grade)*, M. M. Ernst, M.D.

LIVERPOOL REGIONAL HOSPITAL BOARD.—The following Consultant appointments are announced: *Part-time Anaesthetist for St. Helens and Warrington*, P. S. Dearden, M.B., Ch.B., D.A. *Whole-time Senior Radiotherapist at Liverpool Radium Institute*, B. A. Stoll, M.R.C.S., L.R.C.P., F.F.R., D.T.M.&H. *Part-time General Surgeon, at Southport General Infirmary*, C. T. A. Burgess, M.B., B.Chir., F.R.C.S. *Part-time General Surgeon at Sefton General Hospital*, J. G. Gow, M.B., Ch.B., F.R.C.S.Ed. *Part-time General Surgeon for North Wirral Area*, J. A. Shepherd, M.D., Ch.M., F.R.C.S.Ed. *Whole-time Assistant Radiologist at Broadgreen Hospital*, B. B. Harrison, M.B., Ch.B., M.Rad., D.M.R.D. *Whole-time Assistant Radiologist at Mill Road Maternity Hospital*, A. S. Whitehead, M.B., Ch.B., M.Rad., D.M.R.D. *Assistant Radiologist for North Liverpool and Liverpool and District Eastern Hospital Management Committee Groups*, F. B. Wright, M.B., Ch.B., M.Rad., D.M.R.D. *Whole-time Anaesthetist for North and South Liverpool Areas*, Pamela Westhead, M.B., Ch B., D.A.

NORTH-EAST METROPOLITAN REGIONAL HOSPITAL BOARD.—*Full-time Consultant Physician (Physical Medicine), Leytonstone and Romford Groups of Hospitals*, B. E. Brocks, M.B., Ch.B., D.Phys.Med.; *Part-time Consultant General Physician, The Mothers' Hospital (Salvation Army)*, M. Lina Newhouse, M.B., B.S., M.R.C.P.

POWER, PATRICK J., M.B., B.Ch., Assistant Medical Officer, District Mental Hospital, Sligo, Co. Sligo, Eire.

ROUILLARD, L. M., F.R.C.S.Ed., Consultant Plastic Surgeon at Norfolk and Norwich Hospital and United Cambridge Hospitals, East Anglian Regional Hospital Board.

BIRTHS, MARRIAGES, AND DEATHS

BIRTHS

Bailey.—On April 18, 1951, at Greendown, Sonning, Berks, to Nancy, wife of Dr. Grenfell Bailey, a son—Charles Grenfell.

Griffiths.—On April 17, 1951, to Joan, wife of Dr. Donald Barry Griffiths, of Stanmore, a son—Michael John.

Saunders.—On April 9, 1951, at Capetown, South Africa, to Dr. and Mrs. Charles F. Saunders, a sister for Christopher and Margaret.

Smerdon.—On April 12, 1951, at Liverpool Maternity Hospital, to Celia (formerly Tewkesbury), wife of Geoffrey Smerdon, B.M., B.Ch., the Churchill Hospital, Oxford, a daughter.

Teasdale.—On March 21, 1951, at St. James's Hospital, Balham, London, S.W.1, to Elizabeth (formerly Edwards), wife of Derek Hall Teasdale, F.R.C.S., a daughter—Julia Diana.

DEATHS

Agar.—On April 19, 1951, at The Lawn, Henley-in-Arden, Warwicks, Willoughby Agar, M.R.C.S., L.R.C.P., J.P., aged 62.

Comyn.—On April 14, 1951, at 27, Napier Gardens, Hythe, Kent, Arthur Fitzwilliam Comyn, M.B., B.Ch., aged 68.

Games.—On April 11, 1951, at 21, Monton Green, Monton, Eccles, Manchester, John Henry Paisley Games, M.R.C.S., L.R.C.P., aged 62.

Hart.—On April 8, 1951, at Ottery St. Mary Cottage Hospital, Henry Percival Hart, M.C., M.B., B.Ch., Lieutenant-Colonel, R.A.M.C., retired, of Heath Hayes, West Hill, Ottery St. Mary, Devon, aged 70.

Hayman.—On April 14, 1951, George Atkin Hayman, M.R.C.S., L.R.C.P., of 9, Cardington Road, Bedford, aged 72.

Hood.—On April 18, 1951, Martin Crichton Hood, M.R.C.S., L.R.C.P., D.P.M., of West Didsbury, Manchester.

King.—On April 17, 1951, at Hillside, Stratton, Cornwall, Thomas Arthur King, M.R.C.S., L.R.C.P., J.P., aged 78.

Loughlin.—On April 13, 1951, at St. Helier's Hospital, Douglas Loughlin, M.R.C.S., L.R.C.P., of 54, Kinross Avenue, Worcester Park, Surrey.

Mackenzie.—On April 11, 1951, at Druim, Inverness, Theodore Charles Mackenzie, M.D., F.R.C.P.Ed..

McKane.—On April 4, 1951, at Sheffield Royal Infirmary, William Oliphant McKane, M.B., Ch.B.

Olive.—On April 14, 1951, at 19, Kenilworth Road, Leamington Spa, Eustace John Parke Olive, O.B.E., M.D., F.R.C.S.

Playfair.—On April 16, 1951, at New Copse, Fishbourne, Isle of Wight, Ernest Playfair, M.B., M.R.C.P., aged 79.

Rohan.—On April 18, 1951, at a London nursing-home, James Virgil Reynolds Rohan, L.R.C.P.&S.Ed., L.R.F.P.S., L.D.S.Ed., of 32, Coombe Road, Croydon, Surrey, formerly of Mauritius, aged 69.

Ryan.—On April 11, 1951, at his home, Knockrea Park, Douglas Road, Cork, Eugene Ryan, C.M.G., D.S.O., L.R.C.P.&S.Ed., L.R.F.P.S., Colonel, late R.A.M.C., retired, aged 77.

Stewart.—On April 6, 1951, at Vine Cottage, Feock, near Truro, Cornwall, Charles Ravenscroft Stewart, O.B.E., M.B., B.S., D.P.H.

Stockton.—On March 27, 1951, at 7, King's Road, Westcliff-on-Sea, Essex, Hubert Samuel Stockton, M.B., B.S., late of Bromley, Kent, and Peckham, London, S.E., aged 86.

Tracy.—On April 6, 1951, Horace Ernest Humphrey Tracy, M.R.C.S., L.R.C.P., aged 69.

Troup.—On March 30, 1951, at Harefield Sanatorium, Howard Branston Troup, M.R.C.S., L.R.C.P., Squadron Leader, R.A.F., retired, aged 55.

Whitehead.—On April 9, 1951, at Albert House, New Mills, near Stockport, Cheshire, Alfred Whitehead, L.R.C.P.&S.Ed., L.R.F.P.S., aged 78.

Any Questions?

Correspondents should give their names and addresses (not for publication) and include all relevant details in their questions, which should be typed. We publish here a selection of those questions and answers which seem to be of general interest.

Normal Range of Human Temperature

Q.—*What is the reason for the evening temperature usually being higher than the morning temperature? What size of "swing" may be regarded as normal? Do children have a larger or smaller "swing" than adults?*

A.—The inquirer does not specify to which temperature he is referring, oral, axillary, rectal, deep body, or even mean body temperature. There are daily swings in all of these, greater in the rectal and deep temperature, less in the axillary and oral temperatures. The mean body temperature, which is a physical rather than a physiological concept and can be deduced only from other measurements, probably shows the least swing. The two main factors concerned are activity and environment.

The more active an individual is the greater is the amount of metabolic heat produced, and unless this extra heat is lost storage will take place. As the rate of heat loss during activity never quite keeps pace with heat production there is always some rise in body temperature during activity. This rise in body temperature may be, according to Scandinavian workers, of actual advantage to the organism and so should be regarded as a physiological adaptation and not as a fault in control. Even a man resting in bed has a higher metabolic rate than a man asleep, because the former moves around the bed more. Eating also raises the metabolic rate, first because of the physical activity of chewing and swallowing, which, however, is almost too slight to be of significance, and then because of the stimulating effect of food itself, especially protein, on metabolism (specific dynamic action). In these cases also heat loss fails to keep pace with heat production, so there is storage and a rise in body temperature. These processes continuing throughout the waking day result in the slow rise in temperature, taking 10 to 12 hours from morning to night, seen in some individuals.

The rapid fall in temperature on going to bed at night, which is complete in about three hours or less, and the equally rapid rise shown by some individuals on starting the day, are conditioned by changes in the environment. Altering the environment alters the potential rate of heat loss from the body in a given physiological state. The actual rate of heat loss is kept approximately constant and equal to the heat production by changes in the thermal gradients within the body and in the distribution of heat. When comfortable in bed the skin is warm and well supplied with blood; there is only a slight temperature gradient between the centres of metabolism (the sole sources of heat in a resting man) and the skin and superficial tissues; skin temperature is relatively high and the deep body temperature is relatively low. But when the individual gets up, even though he may be fully clothed, his "personal climate" is cooler than when he was in bed, as the thermal insulation of clothes is less than that of the bedding; this, and the effect of cool outside air on exposed parts, causing reflex vasoconstriction elsewhere in the skin, result in a flow of blood away from the skin to the deeper tissues (the analogy might be made with a central heating system and re-routing the hot water from, say, the bedrooms to living-rooms). This redistribution of the blood gives rise to an increased temperature in the deeper tissues, and a decreased temperature in the skin and superficial tissues, as the re-routed warm blood no longer gets a chance to cool off in the skin. The reverse takes place on getting warm in bed at night. In both cases, the aim of these changes being to

keep the rate of heat loss from the body constant, there is approximately no change in the total heat content of the body and so little variation in the mean body temperature.

The diurnal variations demonstrate that the heat-regulating centres in the hypothalamus do not maintain the body temperature at a certain fixed point, represented by "the little arrow on the clinical thermometer," irrespective of all contributing circumstances; but rather they maintain the body temperature within a certain moderately wide range. The centres themselves are apparently concerned in imposing the daily rhythm independent of environment and activity. The usual diurnal temperature curve, with a maximum in the evening and a minimum about 3 a.m., is not established until a child becomes active and starts to walk, but this rhythm, once established, is not readily upset: some shift workers on night work retain the same rhythm as they had when working during the day, although others reverse the pattern to a greater or less extent.

The width of swing varies considerably with different individuals and also the pattern of change. In some, as already mentioned, the rise may be gradual over the whole day; in others the so-called "evening" temperature may be reached a few hours after rising, and there may be no further change for the rest of the day. The pattern usually remains constant in a given individual. The rectal temperature swing is normally between 1 and 2° F. (0.6–1.2° C.), and will be less in a resting than in an active individual; hence it is usually wider in a healthy active child. Oral and axillary temperatures may show less swing than the rectal, as they have a skin as well as a blood component, and skin temperature, in and near the "comfort zone," is affected by environment in the reverse direction to deep body temperature. Unusually wide swings in children are sometimes the result of emotion, which readily affects a child's temperature by altering blood distribution. The regulating centres in young children are very sensitive to water deficiency; hence in hot weather or in warm climates, when an active child may develop a slight degree of "voluntary dehydration" during the day, wider swings may also be found.

For more detailed discussion the inquirer is referred to E. F. Du Bois's monograph, *Fever and the Regulation of Body Temperature* (No. 13, American Lecture Series; Oxford: Blackwell Scientific Publications), and to the late H. C. Bazett's chapter on the regulation of body temperature in Newburgh's symposium, *Physiology of Heat Regulation* (W. B. Saunders, Philadelphia). The whole problem of body temperature and its control is exceedingly complex. If the inquirer finds it difficult to understand he may be consoled by the fact that at a recent international scientific meeting one of the world's leading authorities on body temperature and calorimetry when asked the question direct, "What is body temperature?" answered, "I don't know."

Tonics and Glycerophosphates

Q.—*What precisely is the pharmacological action of a "tonic"? Glycerophosphates are probably the most frequently prescribed tonics, and yet they are said to have no pharmacological action at all. What justification is there for their continued use?*

A.—A tonic may be a substance which increases appetite. Bitter tonics like gentian or liquid extract of nux vomica increase the flow of gastric juice and so increase appetite. The use of alcohol in convalescence has the same justification, though alcohol has drawbacks. The administration of thyroid increases metabolism, and in consequence stimulates appetite. A tonic may also be a substance which helps the subject to overcome excessive placidity and to become more energetic. In this sense the strychnine in Easton's syrup may be said to heighten the activity of the central nervous system. Amphetamine is a tonic in that it removes feelings of fatigue and increases endurance. This is an action on the central nervous system unconnected with appetite, for amphetamine decreases appetite.

Glycerophosphates have no *known* action, but there may be one. We used to think that liquid extract of ergot made according to the 1914 *B.P.* was inert, until ergometrine was discovered. Glycerophosphates may have no action and yet be prescribed as something which is harmless and which has a long tradition. The writer has not met a doctor who was *convinced* that glycerophosphates do good, but there may be many such, and, if there are, he would never deny that their conviction has some evidential value.

Toilet Powders and Respiratory Disease

Q.—*A patient complains of frequent colds and coughs since he has worked in a factory making toilet powders (talcum powder, face powder, etc.). He is engaged in packaging the powder. Is the nature of the man's employment likely to account for his respiratory symptoms?*

A.—Some persons are allergic to orris root, which is often a constituent of toilet powders. Cases of pneumoconiosis due to talc dust in the rubber industry and in the mining and milling of talc are also reported (*Brit. J. industr. Med.*, 1949, **6**, 184).

Damp Brewers' Yeast

Q.—*Brewers' yeast is often supplied damp. Does this cause destruction of the vitamin-B complex?*

A.—If it is supplied wet the yeast may still be alive, and if kept at room temperature may respire or autolyse and use up some of its own vitamins, particularly aneurin. Even from fresh live yeast, moreover, the intestinal absorption of aneurin appears to be less efficient than from dead yeast. For other members of the vitamin-B complex the disparities between live and dead yeast are probably less important. Stable preparations of dried yeast should be readily obtainable, and are to be preferred for nutritional purposes unless the action of the surviving cells in the intestines is considered to be beneficial.

Electric Shock and Damaged Hearts

Q.—*Does the presence of heart disease of any kind make a person more liable to death after an electric shock than a normal person?*

A.—A patient with any form of heart disease liable to result in sudden death from ventricular fibrillation is likely to be hypersensitive to electrical shock. Such diseases include occlusive coronary atherosclerosis, syphilitic aortic incompetence, aortic stenosis, and certain forms of myocarditis (not rheumatic).

Streptomycin Inhalations

Q.—*Are streptomycin inhalations of value in the treatment of pulmonary tuberculosis? If so, what are the dosage and risks?*

A.—There is no evidence that streptomycin inhalations are of any value in the treatment of pulmonary tuberculosis. In particular it has been found that cases of tuberculous bronchitis or tuberculous laryngitis do just as well whether or not streptomycin inhalations are given in addition to intramuscular injections of the drug.

All communications with regard to editorial business should be addressed to THE EDITOR, BRITISH MEDICAL JOURNAL, B.M.A. HOUSE, TAVISTOCK SQUARE, LONDON, W.C.1. TELEPHONE: EUSTON 2111. TELEGRAMS: *Aitiology, Westcent, London.* ORIGINAL ARTICLES AND LETTERS forwarded for publication are understood to be offered to the *British Medical Journal* alone unless the contrary be stated.

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